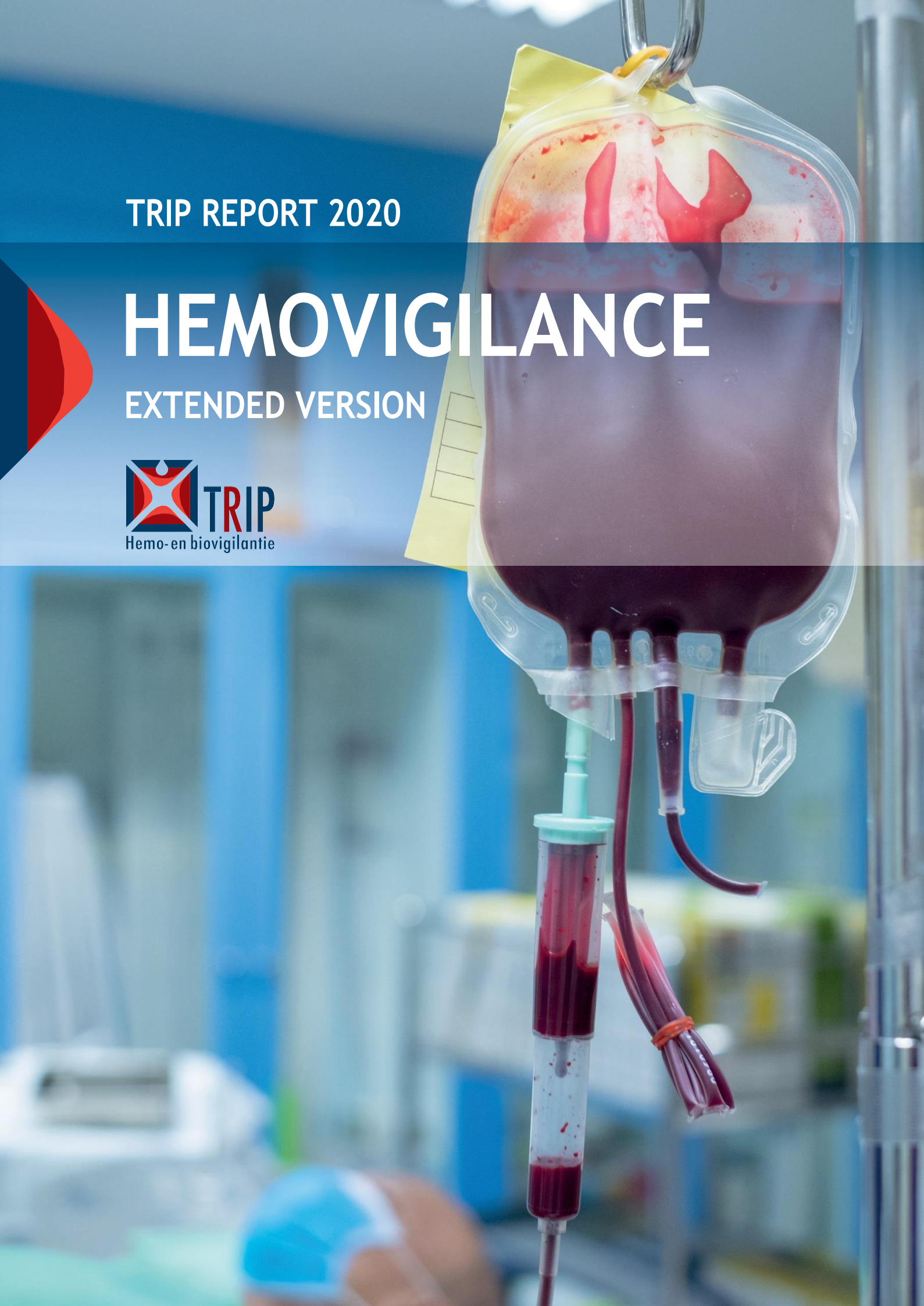
TRIP REPORT 2020

HEMOVIGILANCE

EXTENDED VERSION

TRIP
Hemo-en biovigilantie



TRIP REPORT 2020
HEMOVIGILANCE
EXTENDED VERSION

Hemo- en biovigilantie

TRIP report 2020 hemovigilance, extended version, is published under the responsibility of the TRIP Foundation (Transfusion and Transplantation Reactions in Patients)

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TABLE OF CONTENTS

FOREWORD

Due to the COVID-19 pandemic, 2020 was a special year. Consequently, TRIP Hemovigilance Report 2020 is different from previous reports. What differences would there be in blood use? Were there more or fewer transfusion reactions or incidents? These questions are answered in this TRIP report. The findings show that transfusion practice, like healthcare, has shown itself to be robust. The scaling-down of regular care due to additional care for people with a SARS-CoV-2 infection was accompanied by fewer transfusions and a dip in reports to TRIP in early 2020. In the course of 2020, however, the differences from 2019 became smaller again.

Notable in the findings of the 2020 report is the increased number of serious transfusion reactions (grade 2 or higher). Of these, one third were adverse respiratory events. However, the population of hospital patients was different in 2020, with at least an increased focus on their respiratory condition. Imputability should be taken into account when assessing reports. After analysis, most adverse reactions are somewhere in between 'probable' and 'possible'. Transfusions can be an additional trigger or second hit for transfusion-related acute lung injury (TRALI) in patients with respiratory deterioration, but also the occurrence of transfusion associated circulatory overload (TACO) may be due to additional causes besides the transfusion itself. Further scientific research at all levels will have to show whether more can be learned about the pathophysiology of transfusion reactions with respiratory symptoms. In this context, TRIP aims to better identify the risk factors for these adverse reactions. With such patient-specific knowledge, we particularly hope to be able to reduce adverse events such as TACO. The significance is clear: all grade 4 (fatal) adverse events whose imputability was assessed as certain, probable or possible, involved transfusion associated circulation overload. TRIP will therefore continue to pay special attention to transfusion reactions with dyspnoea in the coming years.

At the time of writing (summer 2021), the pandemic in the Netherlands seems to be on its way out and the use of blood and hemovigilance have largely returned to normal. Words of encouragement and a big compliment are due to everyone in healthcare. Throughout the entire transfusion chain, professionals - from those who collect blood to those who administer transfusions - have done and are doing a tremendous job. It is crucial that we continue to be alert, report and learn together. Things that are different and new may even bring improvements. So let us make good use of this unusual period; it is worth our while to make the transfusion chain even more efficient and safer. I wish you every success in your work.

Jaap Jan Zwaginga,
President, TRIP Foundation

1 MAIN 2020 FINDINGS

1.1 Hemovigilance in 2020

In total, TRIP received 1984 reports of transfusion reactions and incidents in the transfusion chain in 2020. This number is comparable to that of 2019, also relative to the total number of blood components distributed. A decrease in the monthly number of reports was observed in April to June 2020 and can be explained by the scaling down of regular care during the COVID-19 pandemic.

However, there was a higher number of reports of serious transfusion reactions in 2020: 0.28 serious transfusion reactions with definite, probable or possible imputability were reported per 1000 blood components distributed compared to 0.19/1000 blood components in 2019. An increase in severe reactions can be seen in the reporting categories of 'anaphylactic reaction', transfusion-associated circulatory overload' and 'other reaction', with the numbers of severe anaphylactic reactions and circulatory overload reports, which decreased in 2019, at a level comparable to that in 2017-2018 (Table 2, Figure 4, explanation in separate sections in Chapter 3). The increased number of serious other reactions concerns in particular a higher number of reports of serious reactions accompanied by a fall in blood pressure.

Also when looking at the distribution of transfusion reactions of all severity grades, it can be seen that, after a temporary decrease in 2019, anaphylactic reactions and transfusion-associated circulatory overload have increased again in 2020. The number of reports of transfusion-associated circulatory overload in 2020 is comparable to that in 2017-2018. Anaphylactic reactions showed an increasing trend but remained below the level of 2018, while other allergic reactions showed a decreasing trend from 1.2 per 1000 blood components in 2019 to 0.94 in 2020. Other reactions show an increase, such as in the subgroup of reactions associated with dyspnoea. It is likely that the changed hospital population during the COVID-19 pandemic played a role in these shifts. Reactions with respiratory deterioration continue to feature prominently, and attention to prevention of transfusion-associated circulatory overload remains essential.

In the Netherlands, as in other countries, plasma collected from patients who had recovered from COVID-19 (COVID-19 convalescent plasma, CCP) was administered in a clinical study context or on the basis of compassionate use. The number of reactions after administration of CCP, calculated per 1000 distributed units (23), is higher than for standard blood components (relative risk 6.5; 95% confidence interval 3.3 to 12.8). This is possibly (partly) related to the serious condition of the recipients with COVID-19.

Comparing the number of reports received by TRIP to that received by Sanquin has shown that two reactions in 2020 were reported as TRALI (transfusion-related acute lung injury) to Sanquin but not to TRIP. TRALI cases are reported to Sanquin because of the investigation of causative antibodies in donors. This discrepancy in reporting indicates underreporting.

A proposal for revision of the current consensus criteria for the diagnosis of TRALI has been published[1]. The validity and usefulness of the new definition should be established in international collaboraton. As a first step, an international steering committee, in which TRIP is also represented, is working on a uniform reporting form for respiratory transfusion reactions. The aim is global standardization of the assessment of respiratory complications, leading to more evidence-based practice and increasing the safety of transfusions.

[1] Vlaar APJ, Toy P, Fung M, Looney MR, Juffermans NP, Bux J, Bolton-Maggs P, Peters AL, Silliman CC, Kor DJ, Kleinman S. A consensus redefinition of transfusion-related acute lung injury. Transfusion. 2019 Jul;59(7):2465-2476.

In 2020, TRIP did not receive any reports of viral or bacterial transmission through contaminated blood components.

As in other years, the participation in hemovigilance amongst hospitals was high: 79 out of 81 transfusing hospitals (98%) participated. Besides hospitals, there are eight designated institutions in the Netherlands that are authorized to order and administer blood components independently. Of these, five reported on blood components: four reported that no blood components had been administered in 2020, one institution administered only two units to one patient in the whole year. Three of the designated institutions did not provide any figures because the units supplied to them will be reported by the transfusion laboratory of a nearby hospital.

Lastly, the blood group discrepancy project was completed in 2020. This project investigated events that occurred in 2019 and 2020 in which the ABO blood group determined for a patient unexpectedly did not match the previous determination for this patient. The analyses show that correct identification and verification of data is crucial in avoiding and detecting errors. In 44% of the cases analysed, the action that went wrong was identified. Uncovering the cause can reveal risky situations and may result in suggestions for preventive measures.

1.2 Recommendations

Recommendation	Who?
Continued attention to the prevention of TACO. In this context TRIP endorses the recommendation in the Blood Transfusion Guideline 2020 that, in the case of hemodynamically stable patients who are not bleeding acutely, only one unit should be transfused if possible, followed by re-evaluation.	Hemovigilance professionals in collaboration with clinicians.
Ensuring that staff remain competent and capable of applying for and administering blood components, both in a clinical setting and outside the hospital.	Professionals in the transfusion chain and policy makers.
If a blood group discrepancy is found, investigation of the underlying cause. Identifying high-risk situations and implementing improvement measures accordingly.	Hemovigilance professionals in cooperation with all staff involved in requesting, facilitating and performing blood group tests.
Repeated recommendation: Reactions that may be related to donor-specific causes or component quality, for instance with a suspicion of TRALI, should immediately be reported to both TRIP and Sanquin.	Hemovigilance professionals in collaboration with clinicians.

2 OVERVIEW OF 2020 HEMOVIGILANCE DATA

2.1 Overview of 2020 hemovigilance data in comparison with previous years

In 2020, TRIP received 1984 reports. In total, 1821 reactions and 195 incidents (events) were reported; 32 reports concerned a combination of both an incident/event and a reaction. The definitions of categories of incidents, transfusion reactions, severity, imputability etc. can be found on www.tripnet.nl/ under 'definitions' and in the relevant sections of this report.

The reported data are presented in the following tables and figures:

** Supplementary tables available as online annexe*

Table 1 Reported incidents, 2011–2020

Incident	2011	2012	2013	2014	2015	2016	2017	2018*	2019*	2020*	No. of hospitals with reports in 2020
Incorrect blood component transfused	43	51	43	71	53	43	44	41	42	42	22
Near miss	45	50	39	33	40	52	31	35	70	41	12
Other incident	138	139	107	120	93	112	72	94	87	94	23
Calculated risk situation#	-	-	-	-	-	7	6	11	17	8	6
Total	**226**	**240**	**189**	**224**	**186**	**214**	**153**	**181**	**216**	**185$**	**42**

* *All reported incidents have been included, including those registered as an additional category with a reaction.*
\# *The reporting category of 'calculated risk' was introduced 2016.*
$ *Additionally, TRIP received 1 report of look-back and 9 reports with the reporting category or additional reporting category of "bacterial contamination of product' (see Chapter 3.3).*

Table 2 Reported transfusion reactions, 2011–2020

Reaction	2011	2012	2013	2014	2015	2016	2017	2018*	2019*	2020*	≥2# dpp	No. of hospitals with reports in 2020
Post-transfusion bacteremia/sepsis	61	50	47	56	79	64	73	72	84	73[$]	10	36
Post-transfusion viral infection	5	2	5	0	2	3	1	0	0	0	0	0
TRALI	12	9	9	6	9	6	6	4	6	2	2	2
Transfusion-associated circulatory overload	39	56	69	76	76	87	106	134	91	111	39	41
Transfusion-associated dyspnea (TAD)[+]	-	-	-	-	-	8	7	5	4	8	2	5
Anaphylactic reaction	67	59	70	53	43	62	69	58	25	46	27	24
Other allergic reaction	191	180	193	153	151	126	127	134	104	79	1	19
Acute hemolytic TR	17	7	11	17	18	18	16	16	16	13	7	10
Delayed hemolytic transfusion reaction	9	8	4	5	6	8	5	4	3	6	2	6
DHTR as additional category	*19*	*10*	*6*	*8*	*7*	*5*	*3*	*1*	*4*	*7*	*0*	*4*
New allo-antibody formation	831	851	849	763	697	649	672	654	724	598	0	56
Non-hemolytic TR	504	456	442	419	448	407	358	360	317	285	18	57
Mild non-hemolytic febrile reaction	366	383	340	311	336	365	319	327	284	283	2	54
Other reaction	218	225	221	191	205	215	259	288	257	317	30	59
Other small categories of TR[¶]	5	1	5	17	3	4	3	0	3	0	0	0
Total TR	**2325**	**2287**	**2265**	**2067**	**2073**	**2022**	**2021**	**2056**	**1917**	**1821**	**140**	**74**
Total grade 2 or higher#	101	100	108	96	112	108	121	121	104	140		
Total reports	**2630**	**2580**	**2504**	**2318**	**2289**	**2248**	**2131**	**2197**	**2112**	**1984**		

** Reported reactions have been included, including those registered as an additional category with an incident.*
[#] Imputability definite, probable or possible.
[$] None of the reports was categorized as transfusion-transmitted bacterial infection (TTBI) based on the culture result of the unit, see Chapter 3.3.
[+] Reporting category introduced in 2016.
[¶] Concerns reports of post-transfusion purpura, other post-transfusion infection or hemosiderosis.
Abbreviations: TRALI=Transfusion-related acute lung injury; TR=transfusion reaction

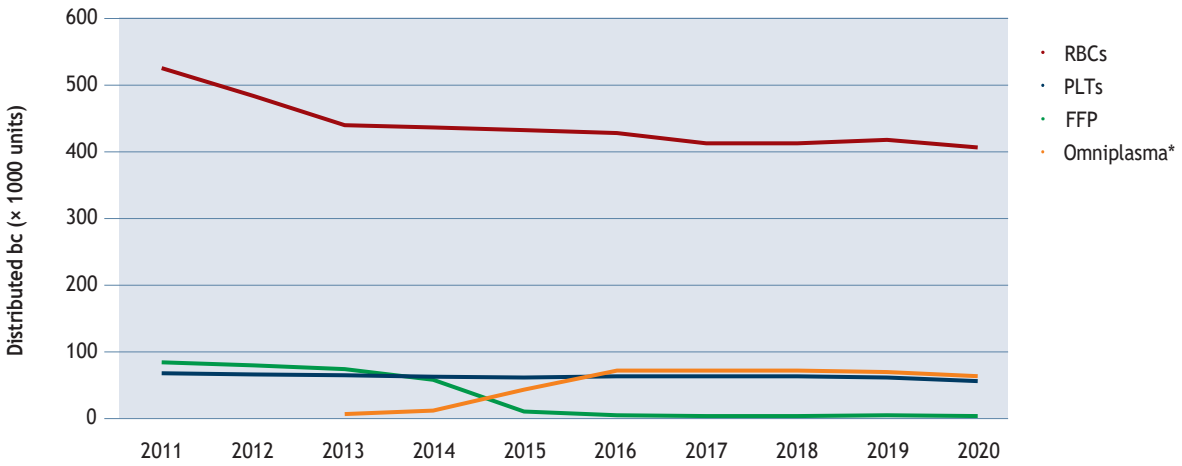

Figure 1 Distributed units of blood components (bc), 2011-2020

For SD-plasma (Omniplasma®), the distributed units have been used in 2013-2015 because of the transition.
(Data from Sanquin)

Table 3 Reports per type of blood component (bc) in 2020

Type of blood component	Units distributed in 2020	Units transfused in 2020[1]	No. of reports		Reports per 1000 bc distributed	
			All	Serious[2]	All	Serious[2]
Red blood cell concentrate	403163	370206	1638	105	4.06	0.26
Platelet concentrate	52042	43669	201	23	3.86	0.44
Fresh frozen plasma	1929	773	0	0	0	0
SD-plasma[3]	52404	39656	13	2	0.25	0.04
Fitrix® fibrin glue	57	30	0	0	0	0
Serum eye drops	586	407	0	0	0	0
Anti-COVID-19 plasma	347	218	8	2	23.05	5.76
Blood management techniques[4]			0	0		
Other blood components[5]			1	0		
Combinations[6]			68	8		
Not stated			55	0		
Total	**508599**	**454959**	**1984**	**140**	**3.89[7]**	**0.27[7]**

[1] Data received from 79/81 hospitals (98%)
[2] Imputability definite, probable or possible
[3] SD=solvent-detergent treated plasma; Omniplasma® in the Netherlands; source Bloedkatern.
[4] See Chapter 3.4
[5] Granulocytes, no indication of administration received.
[6] Including combinations of labile blood components with SD-plasma.
[7] Reports compared to total units of red blood cell concentrates, platelet concentrates, fresh frozen plasma, SD-plasma and units of anti-COVID-19 plasma delivered.

Table 3a **Types of blood component for each type of reaction or incident in 2020**
Table 3b **Types of reactions or incidents for each type of blood component in 2020**

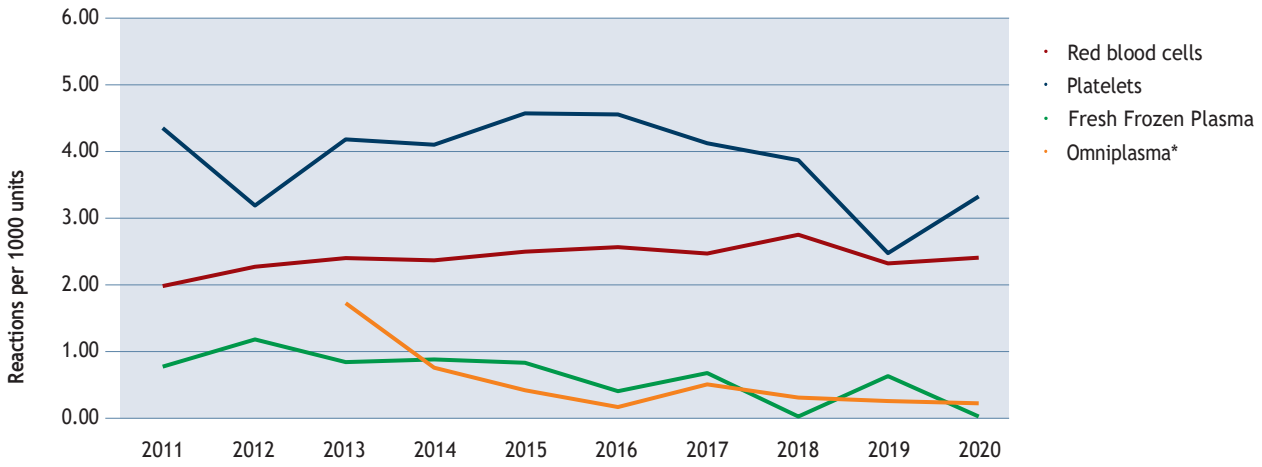

Figure 2 **Transfusion reactions excluding new allo-antibodies per type of blood component, 2011-2020**

This figure displays the transfusion reactions reported with the use of only one type of blood component.
** Omniplasma® (SD-plasma): in 2013-2015 transfused units used as denominator during period of rolling out.*

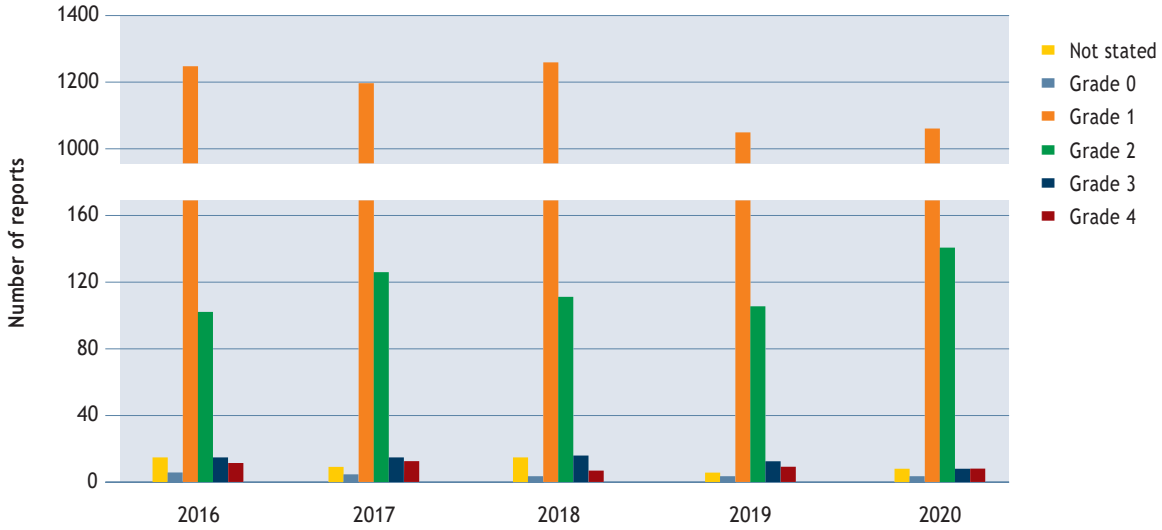

Figure 3 Severity of the transfusion reactions*, 2016-2020

** All transfusion reactions except new allo-antibody formation are included in this figure*

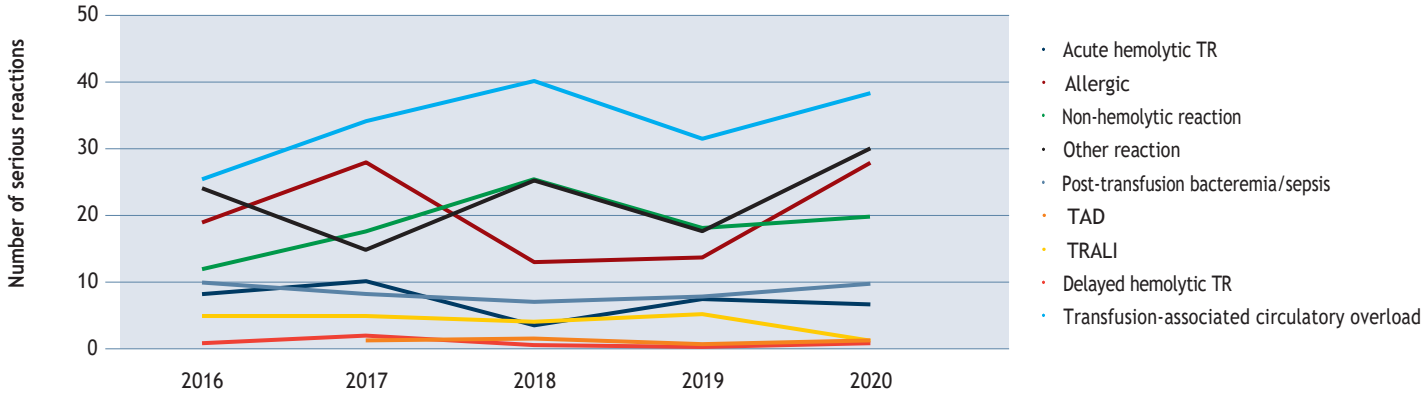

Figure 4 **Serious transfusion reactions (imputability: definite, probable or possible), 2016-2020**

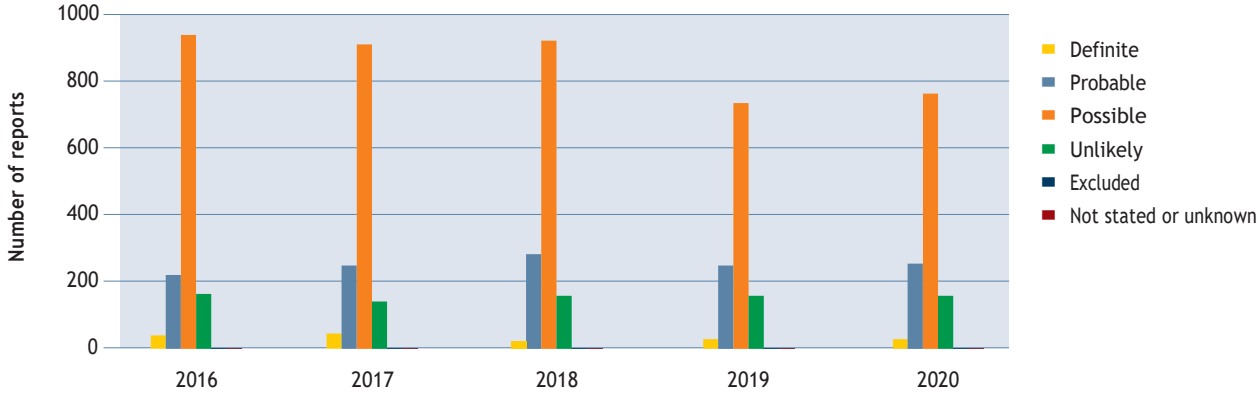

Figure 5 Imputability of the transfusion reactions*, 2016-2020

**All transfusion reactions except new allo-antibody formation are included in this figure.*

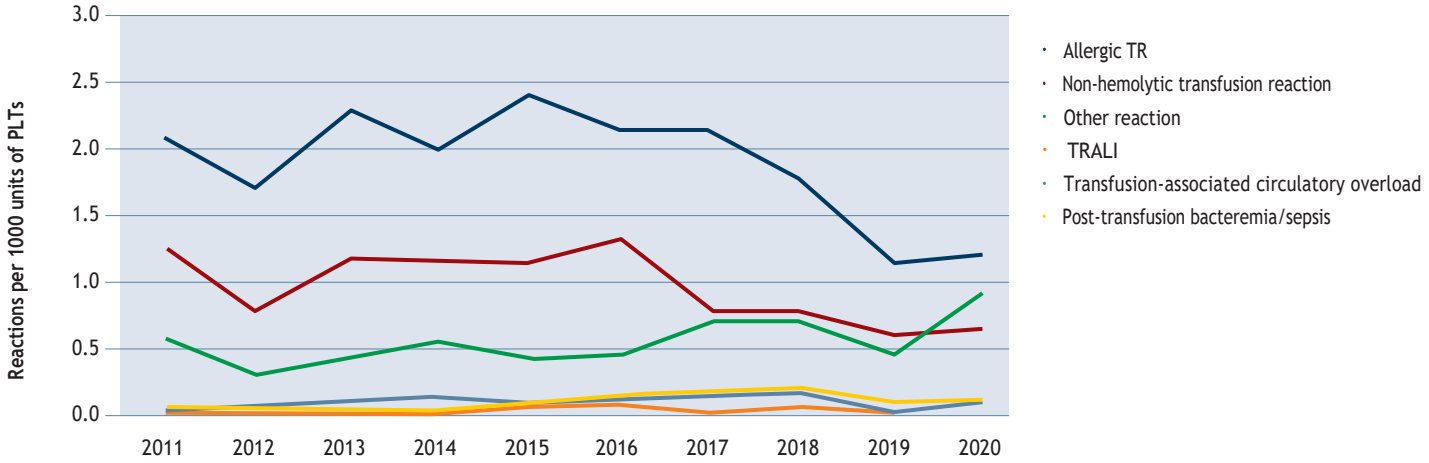

Figure 6a Reactions reported with platelet concentrates, 2011-2020

This figure shows reports from the main reaction categories with definite, probable or possible imputability.*
** In this figure, reactions associated with a combination of types of blood components have been proportionally attributed to the respective types (i.e. a reaction in a patient who received both platelets and red blood cells (RBC) was counted as 0.5 reaction with platelets and 0.5 reaction with RBCs, etc.).*
Abbreviations: TR=transfusion reaction; TRALI=Transfusion-related acute lung injury; PLTs=platelet concentrate.

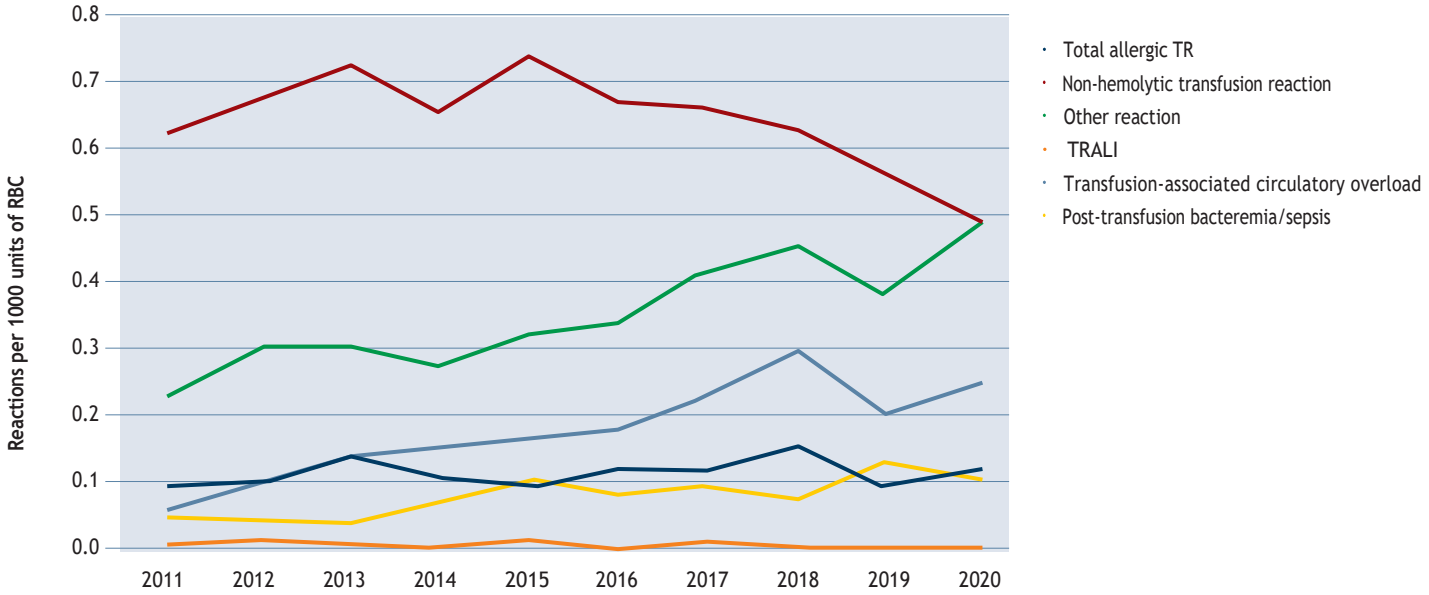

Figure 6a **Reactions reported with red blood cell concentrates, 2011-2020**

This figure shows reports from the main reaction categories with definite, probable or possible imputability.*
** In this figure, reactions associated with a combination of types of blood components have been proportionally attributed to the respective types (i.e. a reaction in a patient who received both platelets and RBC was counted as 0.5 reaction with platelets and 0.5 reaction with RBCs, etc.).*
Abbreviations: TR=transfusion reaction; TRALI=Transfusion-related acute lung injury; RBC=red blood cell concentrate.

2.2 Overview of mandatory reports of serious transfusion reactions to the European Commission

Every year TRIP compiles an overview of mandatory serious transfusion reaction reports (Grade 2 or higher) and incidents in the transfusion chain for the European Commission.

The European Commission gives the following guidance in the 'Common Approach' document:

- Reactions with definite, probable and possible imputability are to be reported; late reports from the previous year are to be included.
- Reactions following transfusion of an incorrect blood component and other incidents are included in the appropriate category.
- Hemolytic reactions are subdivided into immunological (ABO), immunological (non ABO) and non-immunological reactions (e.g. infusion together with hypotonic solution).
- Reactions with only SD-plasma are not included because of the different legal status (medicinal) and vigilance requirements of that product.
- Reports are subdivided in the form according to the type of blood component administered.

The febrile reactions included in the table have been classified as severe due to (prolongation of) hospital admission (Table 4).

Table 4 Number and imputability of reports of grade 2 and higher in 2020 or late reports from 2019, in accordance with EU overview

Severity grade	2 or 3			4		Total
Imputability	Definite	Probable	Possible	Probable	Possible	
Hemolytic transfusion reaction (ABO)		1				1
Hemolytic transfusion reaction (immunological, not ABO)	5	1				6
Hemolytic transfusion reaction (not immunological)			2			2
Allergic reaction	7	10	9			26
Febrile reaction	1	10	10			21
Other reaction	3	10	17			30
TAD			2			2
TRALI			2			2
Transfusion-associated circulatory overload		21	13	1	5	40
Total	**16**	**53**	**55**	**1**	**5**	**130**

2.3 Transfusion reactions with fatal outcome

In 2020, TRIP received eight reports of transfusion reactions after which the patient did not recover and eventually passed away; six of these reports were of probable or possible imputability, two of them were judged to be of unlikely imputability or excluded. These reports are summarized in Table 5. Table 6 lists all Grade 4 reports with definite, probable or possible imputability that TRIP has received from 2010 onwards.

Table 5 Grade 4 reports 2020

Reaction	Sex, age group	Blood component	Imputability	Symptomatology
Transfusion-associated circulatory overload (TACO) saturation	M, 60-69y	RBC	Probable	Hb 2.9 mmol/L, suspected gastrointestinal blood loss; 60% during 2nd unit of RBC, increase in blood pressure, arrhythmia, died.
Transfusion-associated circulatory overload (TACO)	M, 70-79y	RBC	Possible	Cardiac history, acute abdominal pain, Hb 4.4; drop in saturation during 2nd unit of RBC, deteriorated despite oxygen supplementation and diuretics.
Transfusion-associated circulatory overload (TACO)	F, 50-59y	RBC	Possible	Sickle cell anaemia and cardiomyopathy, planned Tf at Hb 4.4 mmol/L; uncomplicated transfusion of 2 units of RBC with furosemide 40mg in between; acute dyspnoea and cardiopulmonary arrest after completion.
Transfusion-associated circulatory overload (TACO)	M, 80-89y	RBC	Possible	Macrocytic anaemia Hb 2.7 mmol/L, elevated BNP before transfusion, in total 4 units of RBC; decreased saturation in the night, pulmonary oedema on CT, no improvement despite furosemide.
Transfusion-associated circulatory overload (TACO)	M, 80-89y	RBC	Possible	Metastasised malignancy, hematuria and sepsis; decrease in saturation, chest X-ray: pulmonary oedema; increased BNP; repeated dips in saturation despite therapy, passed away after a few days.
Transfusion-associated circulatory overload (TACO)	F, 60-69y	RBC	Possible	History of malignancy; complicated course after treatment of dissection; renal impairment; respiratory deterioration after 2 units of RBC, refractory despite diuretics and oxygen administration, died after a few days.
Other reaction	M, 70-79y	RBC	Unlikely	Metastasised malignancy and suspected cholangitis, Tf was terminated after 1 hr 30 min. because of 65% saturation, increase in BP, coughed up blood and died within an hour.
Other reaction	M, 80-89y	PLT	Excluded	Surgery for abdominal aortic aneurysm; platelets after RBC and SD-plasma. In ICU, intubation due to hemodynamic instability, resuscitation terminated because of DNACPR decision.

Abbreviations: M=male; F=female; RBC=red blood cell concentrate; Tf=transfusion; BNP=brain-type natriuretic peptide; DNACPR=do not attempt cardiopulmonary resuscitation.

Table 6 Grade 4 reports (imputability: definite, probable or possible) 2011-2020

Reaction	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
AHTR	1	1			2						4
Other reaction	1	1	2		1	1	1	2			9
Post-transfusion bacteremia/sepsis		1		2							3
Post-transfusion purpura				1							1
TRALI		1			2	1	1	1	1		7
TACO	1	1		3	2	3	6	2	2	6	26
Total	**3**	**5**	**2**	**6**	**7**	**5**	**8**	**5**	**3**	**6**	**50**

Abbreviations: AHTR=Acute hemolytic transfusion reaction; TRALI=Transfusion-related acute lung injury; TACO=Transfusion-associated circulatory overload

2.4 Use of COVID-19 convalescent plasma (CCP) and reports

Plasma collected from patients who have recovered from infection with SARS-coronavirus type 2, COVID-19, and whose levels of anti-COVID-19 antibodies are sufficiently high, may be effective in the treatment of patients with COVID-19. Studies on this subject have been carried out in the Netherlands and internationally, and are still ongoing. In 2020, in the Netherlands, CCP was also administered outside of studies on the basis of compassionate use. Table 7 presents the transfusion reactions reported to TRIP.

Table 7 Reports associated with CCP in 2020

Report	Number	Severity and imputability	Patient
Anaphylactic reaction	1	3 Probable	F, 70-79y
TRALI	1	2 Possible	M, 30-39y
Other allergic reaction	2	1 Definite, 1 Probable	F, 40-59y 2×
Non-hemolytic transfusion reaction	1	1 Probable	M, 70-79y
Mild non-hemolytic febrile reaction	1	1 Probable	M, 60-69y
Other reaction	2	2 Possible	M, 39-39y and 50-59y

Effects of the pandemic on reporting in 2020

On average, there were 165 reactions and incidents per month. The number was lower in the period from April to June (Figure 7). The reports to TRIP do not always contain information on the patient's underlying clinical condition. In total, 29 patients were reported to have COVID-19, in addition to the eight patients who received CCP. The types of reports included three incidents and 26 reactions. In Figure 8, the distribution of transfusion reactions in these patients is plotted against those in patients who did not have COVID-19 or for whom no information on COVID-19 status was given in the report, see also Table 8. There was no difference between the groups in type of blood component, severity of reaction or sex of the patient. In the patients with COVID-19, half (13) of the reactions were recorded as other reactions; this is probably partly due to the features of the underlying disease.

Table 8 Reports concerning patients reported as having COVID-19 (excluding patients treated with CCP)

Report	Patients with COVID-19 (Total 29 reports)			Patients without COVID-19 / unknown (Total 1946 reports)*		
Incidents (including those registered as an additional category with reactions)	3		10%	191		10%
Reactions (including those registered as an additional category with incidents) except new allo-antibody formation	26 reactions See Figure 8			1195 reactions See Figure 8		
Sex	Male	13	50%	Male	623	52%
	Female	13	50%	Female	572	48%
Severity	Severity grade 4	0	0%	Severity grade 4		0.7%
	Severity grade 3	1	4%	Severity grade 3		0.5%
	Severity grade 2		4%	Severity grade 2		12%
	Severity grade 1	24	92%	Severity grade 1		86%
Imputability	Definite	0	0%	Definite	37	3%
	Probable	2	8%	Probable	250	21%
	Possible	16	62%	Possible	745	62%
Type of blood component	RBCs	22	84%	RBCs	959	80%
	PLTs	3	12%	PLTs	173	14%
				SD-plasma	11	0.9%
	Combination	1	4%	Combination	52	4.3%

**Excluding one non-hemolytic reaction after administration of granulocytes.*
Abbreviations: TRALI=transfusion-related acute lung injury; TAD=transfusion-associated dyspnoea; AHTR=acute hemolytic transfusion reaction; CCP=COVID-19 convalescent plasma

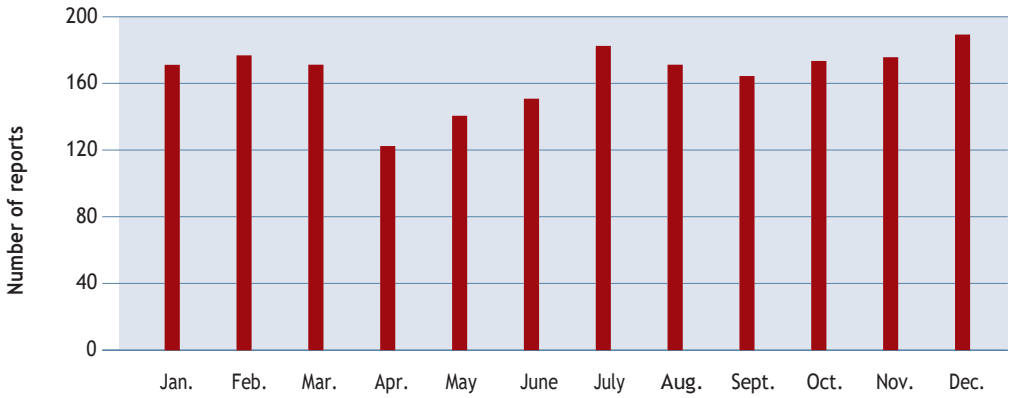

Figure 7 Reports to TRIP of transfusion reactions and incidents per month in 2020

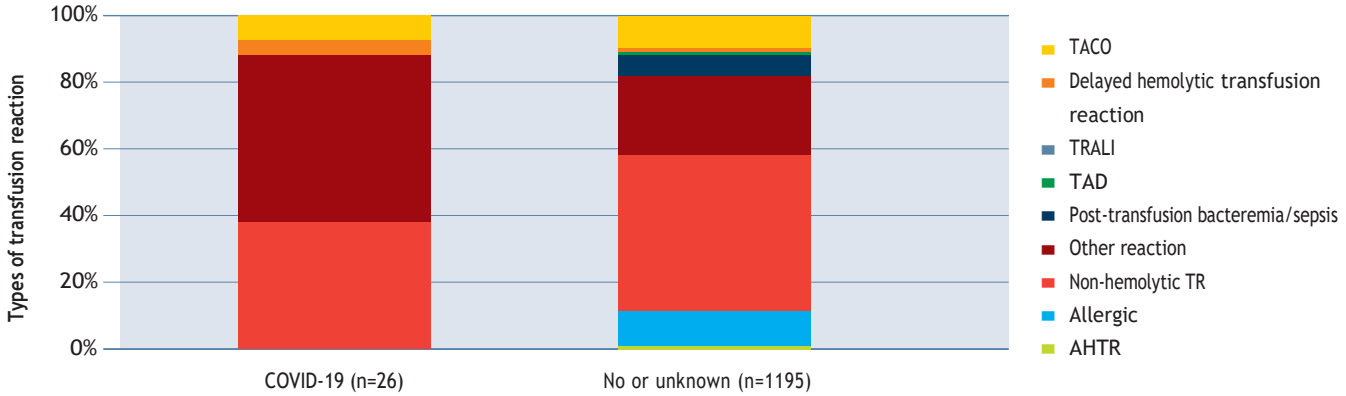

Figure 8 Distribution of types of transfusion reactions* in patients reported to have COVID-19 compared with patients without COVID-19 or not known to have COVID-19 (reports with CCP and new antibody formation are not included).
**Excluding one non-hemolytic reaction after administration of granulocytes.*
Abbreviations: TRALI=transfusion-related acute lung injury; TACO=Transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; AHTR=acute hemolytic transfusion reaction; CCP=COVID-19 convalescent plasma

Conclusion

The COVID-19 pandemic led to a temporary decrease in reports in spring 2020. Eight reactions were reported in reports with the administration of CCP. The number of reported reactions with CCP, calculated per 1000 units distributed (347 units distributed, 23/1000 units), is higher than with standard blood components (Table 3), this might be related to the patients' severe disease state (relative risk 6.5; 95% confidence interval 3.3 to 12.8).

2.5 Late reports from 2019

After the deadline for submitting reports to be included in the 2019 TRIP report, 48 more reports concerning this year were received (from four hospitals) (Table 9). With the exception of two other reactions and one NHTR, all reactions were of definite, probable or possible imputability. Among these, there were three reports of severity grade 2 (one hospital) which, in accordance with the mandatory procedure, will be added to the 2020 statement to the European Commission.

Table 9 Late 2019 reports included in the 2020 report

Reporting category	Severity grade		
	Not stated or 0	1	2
Other allergic reaction		8	1
Mild non-hemolytic febrile reaction		7	
Non-hemolytic transfusion reaction		11	1
New allo-antibody formation	12		
Other reaction		6	
Post-transfusion bacteremia/sepsis		1	
Transfusion-associated circulatory overload			1

3 DISCUSSION OF REPORTS PER CATEGORY

3.1 Incidents in the transfusion chain

Incorrect blood component transfused (IBCT)
All cases in which a patient was transfused with a component that did not fulfil all the requirements of a suitable component for that patient, or that was intended for a different patient.

42 reports, similar to 2019
Number of reporting hospitals: 22 (27%), 1-6 reports per hospital.

- 6x a reaction was observed first and it was discovered afterwards that an IBCT preceded it (see below).
- 18x preventive policy (irregular antibodies and Parvo B19 negative) was not followed, which led to the formation of a new antibody (anti-K) in three cases; 3x transfusion request did not mention that is was for an at-risk patient, 5x problems with ICT aspect (3x 'MISPL' does not work properly, alert for underlying disorder not activated, underlying disorder not processed in all systems), 7x the information was not or only partly read/taken into account during product selection, 1x chronic blood transfusion protocol was not reported to the lab, 1x lab reading error (c instead of C), 1x rhesus phenotyping was manually entered incorrectly (c instead of C).

Description of the risk groups
As in previous years, TRIP assessed all the reports of incorrect blood component transfused to establish which was the worst potential risk to which a patient was exposed through transfusion of an incorrect blood component. The description of the risk groups distinguished TRIP can be found on the website (under Hemovigilance, Supporting materials under Explanations).

In 2020, the largest risk group is 'prevention of irregular antibody formation'. Sixteen of the 41 reports were cases in which the applicable hospital regulations concerning the preventive selection of blood components were not complied with, so that there was a risk of allo-immunisation of patients (Figure 9). This led to the formation of an antibody (anti-K) on three occasions. The downward trend of the ABO risk group in previous years is continuing. The numbers of reports in the rest of the risk groups show little variation. See Table 10 for details.

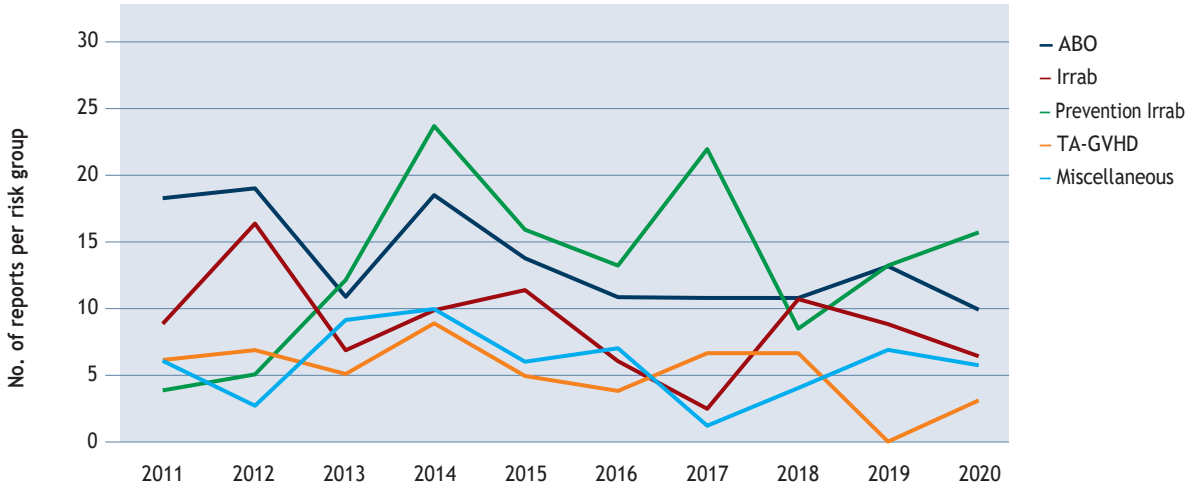

Figure 9 Incorrect blood component transfused 2011-2020: broken down according to risk group

Abbreviations:
ABO = Risk of an ABO incompatible blood transfusion
Irrab = Risk of an irregular antibody incompatible transfusion
Prevention irrab= Risk of alloimmunization due to non-compliance with preventive selection criteria
TA-GVHD = Risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)
Miscellaneous = Administration of a blood bag that has been spiked before (damage/quality; 4); or erroneously not complying with a preventive policy other than the ones named above (B-19 safe; 2)

- Of the ten ABO risk cases, six concern a mix-up of blood bags, patients or patient details. The other four reports concern: patient with stem cell transplant the previous day; removal of a transfusion recommendation after one year due to a technical problem; no checking of patient data at the time of issue and misinterpretation of a weak anti-A. In five cases, this resulted in the administration of an incompatible unit, in two cases the unit was compatible, and in one case it was not clear whether the unit was compatible or not. Furthermore, there was a reaction on two occasions (see below).
- In three of the seven Irrab risk cases, TRIX information or information from third parties on antibodies (detected elsewhere) was present, which could have prevented the error or detected a previously made error, but the information was missed when processing the request. On two occasions, screening for irregular antibodies should have been performed/repeated, but only cross-matching was done, which proved negative. On one occasion, incorrect rhesus phenotyping had been recorded previously for a polytransfused patient. Because of strong changes in the antibody panel, antibody testing was performed by an external party, which detected an anti-c. In the meantime, the patient received another c-positive unit. What led to the entry of the incorrect rhesus phenotype did not come to light. One report stated that, due to a communication error, laboratory staff did not wait for the results of the eluate (anti-Jka). The blood component was cross-matched and administered.

Cases: reactions following IBCT (n=6)

- In connection with a low Hb, a unit of RBC has been requested for a patient. As this patient's blood group has not yet been definitively determined, blood is taken twice on separate occasions for blood group determination. In both determinations, a weak reaction to anti-A reaction is observed. In case of a weak reaction, no automatic conclusion is formulated in the system and the laboratory technician has to enter the conclusion manually. Owing to a misconception the lab technician records blood group A in the laboratory system, whereas the patient has blood group B with anti-A antibodies. A unit of A-positive RBC is prepared and administered to the patient. The patient develops symptoms of dyspnea and general malaise during transfusion, which is terminated. Clinically, the symptoms are attributed to the underlying disease and not the transfusion. The error in blood group determination is discovered when a subsequent transfusion is requested (a few days later) and further investigations are performed. With the updated information, the reaction is diagnosed as an AHTR (severity grade 2).

- One year earlier, the patient (blood group O) exhibited a hemolytic reaction after receiving a unit of platelets (blood group A). The patient system states that they should only receive group O platelets in future. However, the patient receives two units of group A platelets. Half an hour after the second unit has been given, the patient shows a rise in body temperature ≥1 <2 °C; chills/rigors; shortness of breath/dyspnoea and an accelerated pulse/tachycardia. The investigation into what caused the reaction reveals that transfusion recommendations from one year earlier have been removed from the system. Most transfusion recommendations are entered in the system for a defined period. After that period, the system will automatically ask whether the recommendation is to be retained. It is not clear whether that happened in this case. The reaction has been reported in the category of other reaction.
- Four reports concerned new allo-antibody formation (anti-K three times and anti-c once).

- In the three TA-GVHD risk cases, twice the transfusion request fails to mention that they are requests for irradiated units. In the third case the laboratory failed to order an irradiated product as requested. Initially, this error did not seem to have any consequences because by chance an irradiated product seemed to have been delivered by Sanquin. However, this was not the case, there was an error in the laboratory information system. As a result, some product codes incorrectly stated that the unit had been irradiated, while this was not the case. A few weeks after the first incident, this second error came to light when another non-irradiated product was scanned and mistakenly entered into the system as an irradiated product.
- The four damage/quality risk reports relate to three reports of accidental spiking of the blood bag, which was discovered during transfusion, and one case of leakage of the infusion needle, after which the blood component was connected to a new needle.

Table 10 Incorrect blood component transfused in 2020: breakdown according to type of risk, blood component and observed reaction*

Type of risk*	Product	N	Bc compatible by coincidence/negative for	Bc (possibly) incompatible for	N	Reaction or New allo-antibody	N	Imputability	Severity grade
ABO[#]	RBCs	7[&]	Rhesus D	ABO	1	AHTR	1	Probable	2
			ABO rhesus D		6	None			
	PLTs	1	Rhesus D	ABO	1	Other reaction	1	Definite	2
	Plasma	2	N/A	ABO	2	None			
Irrab	RBCs	7		Anti-Jka	1	None			
				Anti-Lea	1	None			
				Anti-c	1	Anti-c	1	Definite	
				Anti-c	1	None			
			Antibodies previously		3	None			
			demonstrated in pt			None			
Prevention Irrab	RBCs	16		Rhesus / K	16				
						None			
Miscellaneous	RBCs	8	Not applicable	Not applicable		Anti-K[%]	3		
	PLTs, RBCs	1	Not applicable	Not applicable		None			
						None			

* *ABO = Risk of an ABO incompatible blood transfusion*
Irrab = Risk of an irregular antibody incompatible transfusion
Prevention irrab= Risk of alloimmunization due to non-compliance with preventive selection criteria
Miscellaneous = Risk by the administration of a blood bag that has been spiked before (damage/quality; 5); or erroneously not complying with a preventive policy other than the ones named above (B-19 safe; 2, irradiated (TA-GVHD); 3).

[#] *One report does not state the blood component.*

[&] *One report mentions RBCs, platelets and plasma.*

[%] *1/3 reports relates to 25 patients, with one IBCT at the time and 24 IBCT in the past; in all a new antibody was formed once (anti-K).*

Abbreviations: Bc = blood component; pt = patient; AHTR = acute hemolytic transfusion reaction

Near miss (NM)
Any error that, if undetected, could have led to a wrong blood group result or issue or administration of an incorrect blood component, and which was detected before transfusion.

41 reports, number of reporting hospitals: 22 (27%), 1-6 reports per hospital.

- Twenty incidents involved a (likely) mix-up of patients or patient data, labels, blood samples, blood components, test materials, etc.
- In 37 reports, there was a potential ABO risk.
- Thirty times the error was detected wholly or partly due to blood group discrepancy.
- The other NMs were detected during planned and unplanned checks, by chance and/or personal alertness (see Table 11).

Table 11 Mode of detection of near misses

Type of risk	N	Subgroup	N	Description	N
ABO	37	Blood group discrepancy	29	— Mix-up of tube/label detected due to blood group discrepancy.	9
				— The laboratory reported several blood group discrepancies with unclear causes, about which the departments were informed.	16
				— Mix-up of patients, discovered due to blood group discrepancy.	1
				— Blood group was identified incorrectly in the past and cause can no longer be determined.	1
				— When requesting unit of PLT, patient's post-SCT status was not communicated to lab; this was discovered by accident due to blood group discrepancy.	1
				— When the patient sticker is scanned, the patient must also be selected.	1
				In this instance, a different person was selected, resulting in the blood results being attributed to the wrong patient (who was not in the hospital).[$]	
		Alertness	5	— The lab called the department to say that the tube with the relevant name had not been received, but a tube with a different name had.	3
				— A&E called to say they had put the wrong sticker on.	1
				— Patient arrived at A&E. Later, parent reported multiple births and patient turns out to have been registered under sister's name. Administrative error corrected.	1
		Clinical situation	3	— Mix-up of tube/label detected due to different blood results than history suggested.	1
				— Test results of the mother were not included in the details of an unborn child; this led to the discovery that the wrong parent had been linked.	1
				— Unexpected positive cross-match.	1
Irrab	1	Wrong data linked	1	— When opening the file on an unborn child, the wrong 'mother' was linked; this was discovered because the wrong mother was 10 years younger and had a different blood group.	1
Traceability	1	Checks at the department	1	— Before attaching the unit, the numbers of the unit and transfusion form were checked and it was found that they did not match. The material was sent back to the lab and the error was corrected. Several units had been prepared for the patient.	1
Preventive irrab policy	2	Rh discrepancy	1	— Rhesus determination in external report does not match the one done in hospital. What caused the rhesus determination in the external report to be incorrect was investigated locally.	1
		Underlying medical condition	1	— Patient's medical condition was overlooked at the lab while they read the transfusion request, this was discovered during a regular check before the unit was finally selected.	1

[$] *Also second report: other incident*
ABO = Risk of an ABO incompatible blood transfusion
Irrab = Risk of an irregular antibody incompatible transfusion
Prevention irrab= Risk of alloimmunization due to non-compliance with preventive selection criteria
SCT = Stem cell transplant
A&E = Accident and Emergency department

TRIP Blood Group Discrepancy Project 2019 and 2020

The TRIP Blood Group Discrepancy Project is based on the fact that a patient's ABO/Rh blood group remains the same, barring exceptions. The detection of a different ABO/Rh blood group from that found in previous determinations is almost always a sign that something has gone wrong somewhere. In most of these cases, the blood tested has not come from the person for whom the test has been requested. Identifying the cause and where possible detecting and addressing underlying factors are of much greater importance than simply reducing the number of cases of blood group discrepancy. Discussing case histories and providing feedback on observed cases will underline the importance of carrying out checks correctly under all circumstances. It will also help to avoid errors or detect them in timely fashion, both within and outside the transfusion chain, where verification of the identifying data is a crucial step.

Of the 104 incidents in which blood group discrepancy was found in 2019 and 2020 and reported to TRIP, 66 fall within the project and contain sufficient information for further analysis (Tables 12 and 13). They include 61 cases detected due to ABO discrepancy in a patient's blood group determinations and three cases with rhesus D discrepancy, while in two reports the type of discrepancy was not known to the reporter. In 49 cases, there was a mix-up, for example of patients, patient data or blood tubes. On three occasions, labels from two patients were mistakenly placed together ('merge'), for example when, after a cancelled request, the label already printed for one patient was not removed but used inadvertently when taking blood from another patient (Table 14). This shows that correct identification and verification of data on each and every label is a crucial action in avoiding or detecting errors. In 44% (29/66) of the cases analysed, the action that went wrong was identified (Table 15). Case studies (in Dutch) discussing these cases in more detail can be found on the TRIP website, under 'supporting materials'.

Table 12 Reports of detected blood group discrepancies 2019 and 2020 (n=104)

	Near miss	Calculated risk	Other incident	Incorrect blood component transfused (IBCT)*	Total
ABO discrepancy[#]	50	1	9	2	62
Rh D discrepancy[&]	8		5		13
Unknown whether ABO or Rh D discrepancy was found	29				29
Total	**87**	**1**	**14**	**2**	**104**

** 1x reporting category AHTR with additional category IBCT*
[#] Including three cases of ABO discrepancy after SCT and one case of an A2 variant blood group, 1x when checking an RBC the blood group determined by the lab (O pos) did not match the bag label (A pos) and the donor was found to be known with a subgroup of A (Ax).
[&] including eight cases of Rh D variant, one case of Rh subtyping discrepancy and one case of Rh D discrepancy after intrauterine transfusion.
Abbreviations: AHTR=acute haemolytic transfusion reaction; SCT= (hematopoietic) stem cell transplantation

Table 13 Was there a mix-up or merge? And which result is wrong? (n=66)

	1st BG result (in past) wrong	1st BG result (current) is wrong	2nd current BG result is wrong	Confirmed (historical) BG is wrong	Current BG check result wrong	No error, BG has changed
Definite mix-up (18) or very likely mix-up (31)	1	3	1		44	
Mistakenly merged (likely)*			1		2	
No mix-up	1	3		2		3
Not identified	3			2		

** * When several tubes of blood were collected from one pt, a label from another pt (left behind) was also used.*
Abbreviations: BG=blood group; pt=pati

Table 14 What was mixed up or merged? (n=52)

Mix-up of patients	3
Patient data (in system)	6
Patient data (label)	9
Mix-up of blood samples	3
Mix-up likely, cause not identified	31

Table 15 What went wrong and how did that happen? (n=66[g])

	Selected wrong pt data during registration	Selected wrong pt data for request	Collected wrong label or labels from several pts together from printer	Mistook pt referred to in blood collection request for someone else	Took extra tube without label	Re-labelled a tube at the lab using a wrong label	Retrieved the wrong tube at the lab	Did not assess/ process/ communicate properly	Different BG result than determination on baby BG card	Cause could not accurately be identified	Total
Blood sample from intended pt but request+label refer to other pt	3	3								13	19
Blood sample from intended pt with label from other pt			5			3				4	12
Pt had paper request form with label from other pt										1	1
Label from intended pt on (remaining) tube of other pt			1	3	1		2			8	15
Test result incorrect								1	2		3
Baby BG in the past differs from the BG of the adult pt										2	2
Incorrect final BG entered into the system								2		1	3
Tf recommendation after SCT not recorded in system								3			3
Not clear										8 (5+3*)	8

Abbreviations: pt=patient; BG=blood group; Tf=transfusion; SCT=stem cell transplant
[g] *including 14 reports with no evidence of mix-ups or accidental merging of data, light blue.*
* *In three cases, a mix-up was a plausible explanation but a previous error in BG determination or recordin BG could not be excluded.*

More descriptions of 2020 Near miss cases with blood group discrepancies (in Dutch) can be found in the Report of the Month series on the TRIP website:
Report of the Month March 2020: Why do things the hard way? …..(3)
Report of the Month November 2020: The label in the lead again - Near miss

Other incident (OI)
Error or incident in the transfusion chain that does not fit into any of the above categories, for instance patient transfused whereas the intention was to keep the blood component in reserve, or transfusing unnecessarily on the basis of an incorrect Hb result or avoidable wastage of a blood component.

- 94 reports, number of reporting hospitals 23 (28%), range of 1-25 reports per hospital, summarized in Table 16.
- 16 cases where a reaction was also observed (4x other reaction; 4x mild NHFR; 3x NHTR, 1x AHTR, 2x TACO, 1x new allo-antibody formation, 1x post-transfusion bacteremia/sepsis).
- One report of a calculated risk with two OIs as an additional category, further described in the following section, is not included in this analysis.

Table 16 Reports of other incidents in 2020, subdivided according to risk group

Type of risk	N	Subgroup	N	Description	N
ABO	4	Possible delay in determining Hb / blood group	3	— Mix-up of tube/label detected due to blood group discrepancy, possibly resulting in delay of operation.	2
				— Mix-up of tube/label detected due to blood group discrepancy, no consequences.	1
		Re-sampling for blood group with possible delay	1	— Wrong patient registered at A&E. Blood group did not match. Error detected after second blood collection.	1
(Preventive policy) Irrab	4	Unrequested / non-standard laboratory results	2	— Rhesus phenotyping before the weekend, followed by transfusion at the weekend. After the weekend, panel was practised outside the protocol, during which an anti-Jkb was found.	1
				— Patient was previously known to have blood group B pos. Today, during the short blood group determination, rhesus D was weak/partial and listed as rhesus D negative for safety's sake.	
		Administration error	1	— Patient known to have cold antibodies was administered warmed units. For the last unit, the heater was not switched on.	1
		Re-sampling for blood group	1	— Wrong patient registered, detected due to blood group discrepancy, consequently, a repeat blood test was required.	1
Damage/quality	22	Wastage of bc	18	— Accidental puncture of unit during spiking.	5
				— Bc collected but Tf cannot take place (yet) due to patient's symptoms.	5
				— Bc collected but Tf cannot take place (yet) or is no longer needed and bc returned to the lab late or not at all.	2
				— Bc collected but Tf cannot (yet) take place or is no longer needed but bc was mistakenly kept unrefrigerated or in the wrong refrigerator.	4
				— IV impaired. The same unit was transferred to a new infusion needle.	1
				— Spike was contaminated by a nurse.	1
		Administration error	4	— Infusion in combination with medication or incorrect infusion fluid. Infusion partly through wrong line.	4

Table 16 (cont'd) Reports of other incidents in 2020, subdivided according to risk group

Type of risk	N	Subgroup	N	Description	N
Under- and/or overtransfusion	40	(Nearly) delay of transfusion	9	— Infusion pump set to incorrect setting (too slow).	2
				— No or incomplete screening/cross-matching so bc was not yet prepared.	2
				— Bc spent longer in OR than intended, but was administered without problems.	1
				— Tf request for a different (incorrect) pt due to mix-up with tube/label for Hb determination, detected later due to blood group discrepancy.	1
				— Tf request for different (incorrect) pt by selecting the wrong pt from the system. This was discovered because the wrong pt had already received transfusion (1) or the nurse did not know anything about a Tf for the patient in question (1).	2
				— During urgent laboratory request, call was not forwarded to walkie-talkie. Furthermore, caller did not wait long enough to be automatically linked to the emergency phone. Non-crossmatched units were issued.	1
		Wastage of (part of) bc	15	— IV impaired and subcutaneous infusion, sometimes with considerable symptoms in the arm/hematoma.	9
				— IV impaired. The same unit was transferred to a new infusion cannula.	1
				— Weakly positive screening. Initially negative screening, therefore cross-matched and administered. During Tf, an anti-M was demonstrated and confusion arose as to whether cross-matching had taken place; bc was therefore disconnected.	1
				— Infusion accidentally disconnected by patient (1) and by nurse (1)	2
				— Tf stopped immediately after observing reaction (mild NHFR), with hindsight unnecessarily.	1
				— Tf started too late and disconnected due to other (scheduled) investigations.	1
		(Nearly) administering unnecessary Tf	11	— Tf based on Hb determination for which a diluted blood sample (drawn from IV arm) was used.	5
				— Tf based on Hb determination for which a coagulated blood sample was used; with other reaction (increase in blood pressure).	1
				— Excessive volume of RBC administered to a child due to inattention.	1
				— (Extra) Tf based on old Hb result. (1x TACO; 1x mild NHFR).	4
		Accelerated transfusion	5	— Infusion pump was set to incorrect setting (too fast) (1x TACO).	5
Traceability	1	Failure in checks/ surveillance of Tf	1	— Registration of administration not according to protocol owing to failure of electronic device which provides an automatic identification from bc to pt.	1
Other	23	Reaction not reported to lab or reported too late	6	— Symptoms during or at the conclusion of Tf, not reported or reported too late to the laboratory. 1x Other reaction, 3x (mild) NHFR, 1x Post-transfusion bacteremia/sepsis.	6
		Wastage of (part of) blood component	9	— Accidental puncture of unit or bc collected but Tf could not (yet) take place or was no longer needed.	3
				— Bc had a variant blood group which created a discrepancy between the blood group determinations at the hospital and the reference laboratory, and the bc was returned.	1
				— Blood component had partially infused subcutaneously.	1
				— Accidental puncture of unit during spiking.	1
				— Blood results of pt during transfusion showed AIHA. Transfusion is stopped.	1
		Administration error	4	— Infusion rate adjusted without consultation.	1
				— Infusion pump set to incorrect setting (too slow)	2
				— Bc was not connected within 30 minutes	1
		Possible delay in determining Hb / blood group	3	— Mix-up with tube/label for Hb/blood group determination, detected due to a blood group discrepancy (1) or by observant doctor (1)	2
				— When the patient sticker is scanned, the patient must also be selected. In this instance, a different person was selected, resulting in the blood results being attributed to the wrong patient (who was not in the hospital).[$]	1
		Miscellaneous	1	— Returned bag not properly packed; risk of contaminated culture result.	1

[$] *Also second report: Near miss*
ABO = risk of an ABO incompatible blood transfusion
Irrab = risk of an irregular antibody incompatible transfusion
Prevention irrab = risk of alloimmunization due to non-compliance with preventive selection criteria
Abbreviations: Tf=transfusion; pt=patient; bc=blood component; AHTR=acute hemolytic transfusion reaction; NHFR=non-hemolytic febrile reaction; TACO=Transfusion-associated Circulatory Overload; AIHA=autoimmune hemolytic anaemia.

A number of '2020 Other incident cases' have been described in the Report of the Month series on the TRIP website:
Report of the month April 2020: Were preventive measures successful in preventing TACO?
Report of the month October 2020 To measure is to know(2)
Report of the Month 2021 – 1: Should new allo-antibody formation be reported?

Calculated risk situation
A situation where the clinician knowingly decides to proceed with transfusion in the presence of an increased risk or anticipated side effect of the transfusion and where the intended benefit from transfusion is deemed to justify the risk of harm and its possible severity.

8 reports, number of reporting hospitals: 6 (7%), 1-2 reports per hospital.
- 1 report of new allo-antibody formation in a Calculated risk situation
- 2 reports with additional category of Other incident, because the clinical chemist had not been informed.

In five cases, the reports of calculated risk situations in 2020 concerned emergency situations in circumstances which did not allow for consideration of irregular antibodies previously demonstrated in a patient (n=5), Three reports involved patients with massive blood loss who received non-crossmatched units. The last two cases (concerning one patient) involved an emergency situation in which two non-crossmatched units were issued and administered. The patient had a positive antibody screening. The clinical chemist was not informed that no antibody screening had been performed and (with hindsight and according to hospital protocol) this should have been done (other incident).

Three of the cases did occur in an emergency situation. These cases concerned calculated risks according to the hospital protocol and permitted working methods. These occurrences are not errors, but are nevertheless worth pointing out. TRIP is investigating how best to classify these reports in future in order to draw lessons from relevant cases. One report concerned a patient for whom units had been prepared. However, between the processing of the request and the collection of the units, the blood results based on manual leukocyte differentiation changed, resulting in an indication for irradiated units. The prepared (non-irradiated) unit was administered; in accordance with laboratory procedure, the adjusted laboratory result did not have to be passed on. In a second case, the patient underwent an allogeneic stem cell transplant. In accordance with protocol, transfusion after a stem cell transplant must be compatible for Kell and for previously known allo-antibodies. Patient was not known to have anti-E before stem cell transplantation but it is present after transfusion. The third case concerned a patient who showed a negative screening one day before transfusion; two units were issued on type & screen. On the morning before transfusion, another screening was performed. This showed a weak positive reaction (anti-Jkb). The positive test result was found when the first unit had already been given (homozygous Jkb positive). The second unit given was compatible.

3.2 Non-infectious transfusion

Respiratory transfusion reactions

Transfusion-associated Circulatory Overload (TACO)
Respiratory problems during or within 12 hours after transfusion, manifested by at least one pulmonary feature (criterion A or B). In all, at least 3 of the criteria below must be met.
See notes 1 to 6 on www.tripnet.nl.

A New or worsening respiratory problems (see note 1)
B Features of new or worsening pulmonary oedema, based on:
— Physical examination (see note 2), and/or
— Chest X-ray or other imaging of the chest (see note 3)
C Relevant changes in the cardiovascular system (see note 4)
D Findings suggestive of relevant changes in fluid balance (see note 5)
E Biomarker result(s) consistent with TACO (see note 6)

- 111 TACO reports, 41 of which were of severity grade 2 or higher.
- 41 reporting hospitals (51%), 1 to 11 reports per hospital.
- Twice TACO was reported together with another incident, during which overtransfusion occurred.
- 14 times TACO was registered with a different type of reaction in the additional category due to additional findings that did not fit TACO. In addition, TACO was recorded 5 times as an additional category with another type of transfusion reaction. The types of reactions recorded together with TACO are in total: 11 non-hemolytic reactions, five post-transfusion bacteremia/sepsis, two other reactions and one anaphylactic reaction.
- Severity and imputability of all TACO cases in reporting and additional categories are summarized in Table 17.
- Median age of patients: 76 years (range 4 to 97).

Transfusion-associated circulatory overload occurred after transfusion of RBCs (n=107), sometimes in combination with platelets (n=4), SDP (n=1) or both (n=1), in cases of extensive blood loss. TACO occurred three times after administration of platelet units only and once after administration of SDP.

In line with previous years, TACO was the transfusion reaction with the highest number of serious reports (Table 2), and the reaction that most frequently led to the death of patients (Table 5). Both in terms of numbers and severity, an increase in the number of TACO reports was observed compared to 2019, also when these numbers were plotted against the number of blood components used. The level in 2020 is similar to the results in 2017-2018 (Table 2, Figure 4). Thus the downward trend observed in 2019 did not continue.

Transfusion-associated circulatory overload is considered a potentially avoidable complication. Although the pathophysiology of TACO is not exactly known, several measures have been introduced to reduce its risk. Risk groups have been identified, and recommendations have been made for the administration of blood components to high-risk patients, such as administering a diuretic prior to transfusion and adjusting the transfusion rate. The TRIP TACO prevention tool, with separate versions for doctors and nurses, guides risk assessment and draws attention to these preventive measures. The revised Dutch Blood Transfusion Policy Guideline also recommends that patients who are not bleeding acutely, and who are hemodynamically stable, should be transfused with just one unit if possible, to be followed by an Hb check.

In order to get a good picture of the incidence of avoidable factors in the transfusion chain, reports of all severity levels should be reviewed. Even if the onset of TACO is recognised in time and the severity of the reaction remains limited, the case can provide valuable information, and reporting is of added value. Given the incidence and severity of respiratory complications, TRIP will pay extra attention to cases of dyspnoea in the years to come.

A number of 2020 TACO cases have been described in Dutch in the Report of the Month series on www.tripnet.nl, e.g. Report of the Month 2021 – 2: Transfusion reaction with fever and dyspnoea

Table 17 Severity and imputability of all TACO cases in 2020 (in reporting or additional categories)

Imputability		Severity grade			
	Total number of reports*	1	2	3	4
Definite	2	2			
Probable	52	30	20	1	1
Possible	57	39	11	2	5
Unlikely	3	1	2		
Total	**114***	**72***	**33**	**3**	**6**

* The imputability of two grade 1 reports was not assessed

TRALI (Transfusion-related Acute Lung Injury)

Dyspnoea and hypoxia within six hours of the transfusion; chest X-ray shows bilateral pulmonary infiltrates.

- Two TRALI reports in 2020, both with possible imputability and severity grade 2.
- One TRALI after administration of RBC in combination with SD-plasma, one TRALI after administration of fresh frozen CCP in a patient with COVID-19.
- In addition to these two reports, two reactions were reported to Sanquin as suspected TRALI, which were not reported to TRIP either as TRALI or in another reporting category, see comment in Chapter 4.

TRALI is a rare but potentially life-threatening complication of transfusion of blood components. The diagnosis is based on clinical presentation and should be supported by appropriate radiological findings.

The etiology of TRALI is multicausal; the pathogenesis often explained by a "two hit" hypothesis. The first hit in this model is patient predisposition, where inflammatory pathological conditions or external factors activate the pulmonary vascular endothelium and prime neutrophils[1,2,3]. Transfusion is the second hit, where it is assumed that immunological triggers, the passive transfer of donor leukocyte antibodies and/or the infusion of biological response modifiers, are associated with the occurrence of TRALI[3].
There are indications of patient predisposition in both reports in 2020 (see boxes).

A female patient was administered three RBC units and two SD plasma units in a short period of time in connection with a hemorrhage during abdominal surgery. Possible predisposing factors: Recent surgery and transfusion of five blood components.

A COVID-19 positive male patient with pneumonia was administered convalescent plasma. Possible predisposing factor: Pneumonia.

[1] Vlaar APJ, Toy P, Fung M, Looney MR, Juffermans NP, Bux J, Bolton-Maggs P, Peters AL, Silliman CC, Kor DJ, Kleinman S. A consensus redefinition of transfusion-related acute lung injury. Transfusion. 2019 Jul; 59(7):2465-2476.
[2] Tariket S, Sut C, Hamzeh-Cognasse H, Laradi S, Pozzetto B, Garraud O, Cognasse F. Transfusion-related acute lung injury: transfusion, platelets and biological response modifiers. Expert Rev Hematol. 2016 May ;9(5):497-508.
[3] Popovsky M. Transfusion reactions, 4th edition. 2012. ISBN :9781563958359.

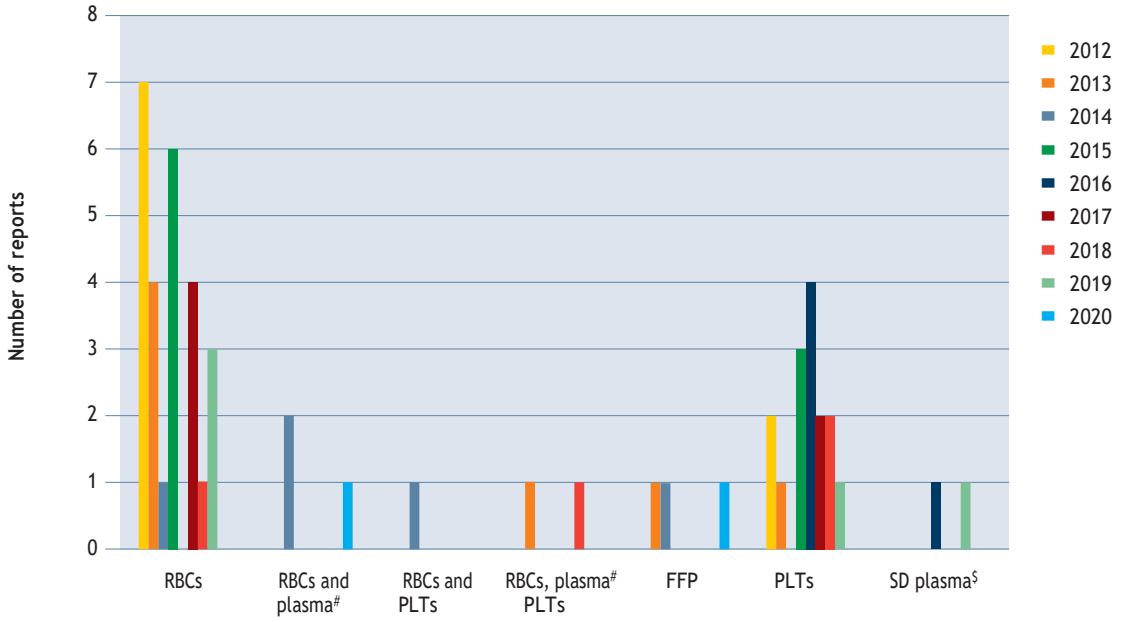

Figure 10 Type of blood component in TRALI reports of certain, probable or possible imputability, 2012-2020
 # The plasma was FFP up to 2014 and SD-plasma from 2016 to 2020.
** The FFP was quarantine fresh frozen plasma in 2013-2014 and COVID-19 convalescent plasma in 2020.*
$ TRALI in 2016 concerned a patient with risk factors for ARDS, and TACO could not be excluded.

A proposal for revision of the current consensus criteria for the diagnosis of TRALI was published internationally in 2019[1]. The validity and usefulness of the new definition in hemovigilance should be established in international cooperation. As a first step, an international steering committee is working on a uniform reporting form for respiratory transfusion reactions. The aim is global harmonization of the assessment of these types of reactions, leading to more evidence-based practice, better recognition, and safer transfusions. TRIP is actively contributing to this work.

Transfusion-associated dyspnoea (TAD)

Shortness of breath or hypoxia during or within 24 hours after a blood transfusion, and the criteria for TRALI, circulatory overload, or anaphylactic reaction are not met. Respiratory problems are the most prominent feature and they cannot be explained by the patient's underlying pathology or other known specific causes.

- Eight reports, six with severity grade 1 and two with severity grade 2.
- A total of 32 reports since this reporting category was introduced in 2016 (Table 18).

Inherent to the definition of TAD is that dyspnoea is not explained by known underlying factors. In reactions where dyspnoea is the most prominent symptom, other causes for respiratory problems should be considered after ruling out TRALI, TACO and anaphylactic reaction. If underlying pathology can be demonstrated, the report is categorised by TRIP as 'other reaction with dyspnoea'. The pathophysiology of TAD remains unexplained. It is conceivable that cases represent a less severe form of TRALI or TACO that does not meet the criteria for those reactions. Research into the nature of this type of reaction is necessary to enable appropriate prevention.

Table 18 Transfusion-associated dyspnoea (TAD), 2016-2020

TAD N=32	Reporting hospitals: 18
Age	Median 63y, range 14-84y
Sex	16 F, 16 M
Interval	Interval median 1 hr 23 min, range 7 min to 6 hrs 40 min
Previous Tf and/or pregnancy	Previous Tf known in 13/16 female patients, previous pregnancy known in 8/16 female patients
	Previous Tf known in 15/16 male patients
Severity grade	7x grade 2, 25x grade 1
Imputability	6 probable, 24 possible, 2 unlikely
Symptoms	31 Dyspnoea and/or decrease in oxygen saturation
	19 Increase in temperature and/or chills
	6 systolic ≥30 mm Hg (<50 mm Hg) increase in blood pressure, diastolic increased max. 25 mm Hg
	4 systolic ≥20 mm Hg (<40 mm Hg) increase in blood pressure, diastolic decreased max. 13 mm Hg
	1 Cough
	8 Tachycardia
	3 Restlessness, malaise
	2 Chest pain
	4 Wheeze/stridor
	Other symptoms: 1x headache, 1x pain in the flank

Conclusion respiratory transfusion reactions

Respiratory transfusion reactions are a major cause of transfusion-associated morbidity and mortality. In 2020 as in previous years, TRALI, TACO and TAD together accounted for the highest number of serious reports and most transfusion-related deaths. These respiratory complications can be difficult to distinguish from each other and from other transfusion reactions with dyspnoea such as anaphylactic reactions. Given their incidence and importance, TRIP will pay extra attention to respiratory transfusion complications in the coming years.

Acute hemolytic transfusion reaction (AHTR)

Signs or symptoms of hemolysis occurring within a few minutes of commencement or until 24 hours after a transfusion, such as a drop in systolic and/or diastolic blood pressure of ≥20 mm Hg, fever/chills, nausea/vomiting, back pain, dark or red urine, no or poor increase of Hb level or an unexpected drop in Hb.

- 13 reports, including one with unlikely imputability in a patient also suffering from medication-induced hemolysis; this is not discussed further.
- 11 with RBC, including one case in which also platelets were transfused and one case in which also plasma was transfused; one with platelets only.
- One AHTR with severity level 2 due to ABO incompatible transfusion, discontinued at symptom onset 8 min after start of transfusion (IBCT was recorded as additional category).
- Two reports concerned a patient with non-specific cold and warm antibodies, which meant that no serological conclusion could be drawn about specific irregular antibodies. Subsequent transfusions using a blood warmer were uncomplicated.
- Two reports concerned a patient (with undetected irregular antibodies), in which both blood components were positive for the antigen corresponding to the antibody which the patient had developed. These reports record an additional category of other incident and new allo-antibody formation, respectively. This case has been described as Report of the Month.

Table 19 Acute hemolytic transfusion reaction (AHTR) in 2020

AHTR N=12	Reporting hospitals: 9
Age	Median 77y, range 0-81y
Sex	6 Female, 6 Male
Interval	Interval median 1:55 hr, range 8 min 5 days
Previous Tf and/or pregnancy	Recorded in 4/6 male patients, 4/6 female patients with AHTR Pregnancy 3x previous, 1x none, 1x unknown, 1x not stated
Severity grade	7x grade 2, 5x grade 1
Cause	1x patient with (suspected) paroxysmal nocturnal hemoglobinuria 1x no cause found; possibly medication-induced hepatitis 1x no cause found; possibly antibodies in unit of platelets 1x patient received donor plasma with IgM hemolysins and agglutinins 1x patient with (suspected) auto-immune hemolytic anaemia 1x patient with ABO incompatibility (additional category: IBCT) 3x patient with undetected irregular antibodies (anti-Jka and anti-Wra) 1x patient with anti-A1 2x same patient with specific cold and non-specific warm autoantibodies, hence no serological conclusion (see above; report of the month)
Imputability	4x definite, 3x probable, 5x possible

Delayed hemolytic transfusion reaction (DHTR)

Signs or symptoms of hemolysis occurring within a few minutes of commencement or until 24 hours after a transfusion, such as unexplained drop in Hb, dark urine, fever/chills.

- Thirteen reports (all associated with RBC transfusion)
- Six reports of DHTR, four of which had 'New allo-antibody formation' as additional category (twice anti-Jkb, once anti-E and once anti-E and anti-K)
- Seven reports of 'New allo-antibody formation' with DHTR as additional category
- Preventive measures are the matching of RBC transfusions in accordance with the Blood Transfusion Policy Guideline, as well as the use of TRIX (national transfusion registry for irregular antibodies and cross-match problems).
-

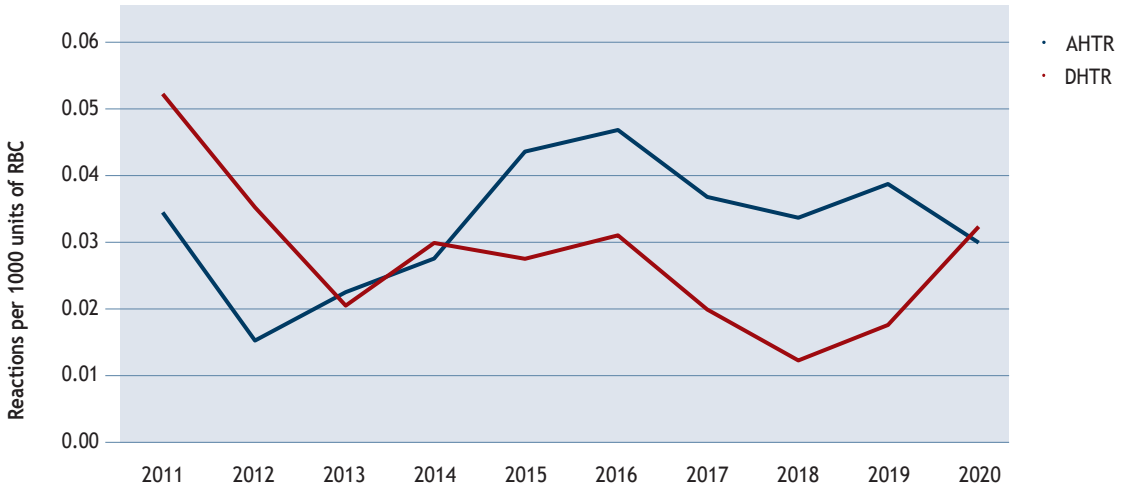

Figure 11 Reports of acute and delayed hemolytic transfusion reactions relative to the number of red blood cell concentrates (RBC) distributed, 2011-2020
Encompasses all reports with definite, probable and possible imputability, including hemolytic reactions with incorrect blood component transfused or demonstration of new allo-antibody formation

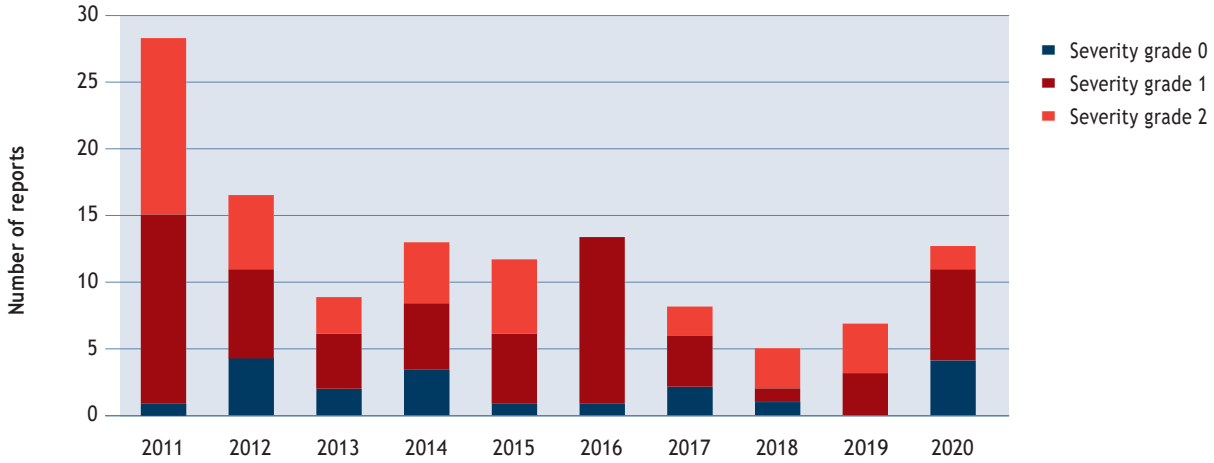

Figure 12 Severity of reports of DHTR (main/additional category; imputability definite, probable, possible), 2011-2020

Anaphylactic reaction and other allergic reaction

Anaphylactic reaction
Rapidly developing allergic reaction occurring within a few seconds after the start of transfusion or up till a short time after transfusion with features such as stridor, fall in systolic and/or diastolic blood pressure ≥20mm Hg, nausea/vomiting, diarrhoea, back pain, skin rash.

Other allergic reaction
Allergic phenomena such as itching, redness or urticaria without objective respiratory, cardiovascular or gastrointestinal features, arising from a few minutes of starting transfusion until a few hours after its completion.

- A total of 125 reports of anaphylactic and other allergic reactions (46 and 79, respectively), compared to 125 reports (25 and 100, respectively) including late reports in 2019 (Figure 13).
- Number of reporting hospitals: 40 (49%), range: 1-17 reports per hospital.
- The number of reports (n=27) of severe anaphylactic reactions (grade 2 and higher) with definite, probable or possible imputability was higher than in 2019 (11 in 2019), but is within the range of fluctuations in recent years (Figure 4).
- 17 reports of allergic reaction contained the information that an IgA determination had been carried out within the context of the transfusion reaction. Not all patients with an IgA deficiency develop antibodies against IgA and not all patients with anti-IgA show transfusion reactions. With 7 reports in categories other than the allergic category, an IgA determination was carried out.
- In 2020, there were two reports indicating the presence of anti-IgA. One concerned a severe anaphylactic reaction during transfusion of platelets for which oxygen, clemastine, hydrocortisone and two doses of adrenaline were administered. The other reaction where the presence of anti-IgA was confirmed was in an IgA-deficient patient with a mild non-hemolytic febrile reaction after an RBC transfusion.
- 6 times an anaphylactic reaction was reported (5x severity grade 2) in the same patient.
- Nine times an other allergic reaction was reported in the additional category, 1x with mild NHFR, 3x with a non-hemolytic transfusion reaction, 3x with post-transfusion bacteremia/sepsis, 2x with Other reaction.
- Information on the cases is summarized in Table 20.

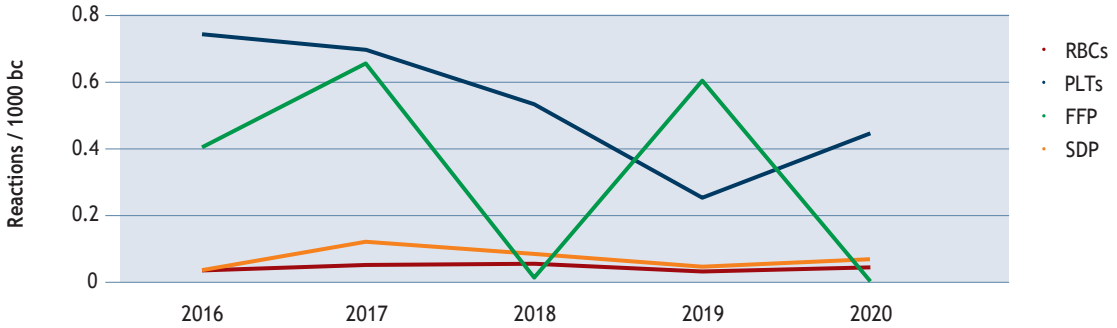

Figure 13a Number of anaphylactic transfusion reactions relative to the numbers of blood components (bc) distributed, 2016-2020

** In this figure, reactions to a combination of types of blood components have been proportionally attributed to the respective types (i.e. a reaction in a patient who received both platelets and RBC was counted as 0.5 reaction with platelets and 0.5 reaction with RBC, etc.).*

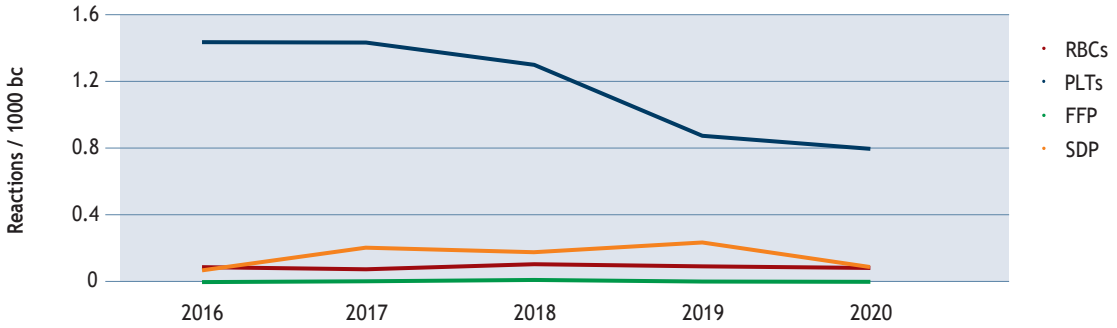

Figure 13b Number of other allergic reactions relative to the numbers of blood components (bc) distributed, 2016-2020

** In this figure, reactions to a combination of types of blood components have been proportionally attributed to the respective types (i.e. a reaction in a patient who received both platelets and RBC was counted as 0.5 reaction with platelets and 0.5 reaction with RBC, etc.).*

Table 20 Overview of reports of anaphylactic reactions and other allergic reactions

	Anaphylactic reaction		Other allergic reaction	
Number of reports	46		79	
Age average, median (IQR)	53 years, median 51.5 (IQR 35-70)		44 years, median 50 (IQR 15.5-66.5)	
Sex	19 Female (41%)		39 Female (49%)	
Serious	27 serious, of which 27 with definite, probable or possible imputability		1 serious with possible imputability due to admission for observation	
Product	**Number (% of total)**	**Reports per 1000 units**	**Number (% of total)**	**Reports per 1000 units**
Red blood cell concentrate	16 (35%)	0.04	30 (38%)	0.07
Platelet concentrate	24 (52%)	0.46	40 (51%)	0.77
FFP	0		0	
SD-plasma	3 (7%)	0.06	3 (4%)	0.06
Convalescent anti-COVID plasma	1 (2%)	2.88	2 (3%)	5.76
Multiple types (labile bc and possibly SD-plasma)	2 (4%)		4 (5%)	
Symptoms (number of reports):				
Skin symptoms:				
Itching, urticaria, redness	23		79	
Glottal oedema	9		-	
Increase in temperature:				
1-2 ˚C	6		7	
≥2 ˚C	2		5	
Chills	8		7	
Unresponsive / less responsive	3		-	
Dyspnoea/decrease in oxygen saturation	26		2	
Stridor/ bronchospasms	7		-	
Decrease in blood pressure	21 (9x ≥20 mm Hg syst and/or diast)		-	
Increase in blood pressure	4 (3x ≥20 mm Hg syst and/or diast)		1	
Nausea/vomiting/diarrhoea	6		2	

New allo-antibody formation

After receiving a transfusion, demonstration of clinically relevant antibodies against blood cells (irregular antibodies, HLA or HPA antibodies) that were not present previously (as far as is known in that hospital). As of 2021 cases should only be reported to TRIP in special circumstances, e.g. in combination with a transfusion reaction, (suspected) haemolysis and/or antibody formation due to incorrect blood product selection.

- 598 reports (610 including reports with new allo-antibody formation as an additional category), 705 new allo-antibodies
- Number of reporting hospitals: 58 (72%), 1-50 reports per hospital
- 238 M and 372 F, including 33 new antibodies in women < 45 years of age at the time of transfusion
- Specificities displayed in Table 21
- Formation of anti-c, anti-E or anti-K in 11 women <45 years old (Table 22), one report of incorrect selection of blood components with this subgroup.

Table 21 New allo-antibodies in 2020: Most frequent specificities in women and men

New antibody	F<45y*	F total	M	Ratio F/M	Percentage (TRIP 2020)	TRIX#
anti-E	5	137	86	1.6	31.6%	16.7%
anti-K	2	96	65	1.5	22.8%	12.9%
anti-Jka	1	29	21	1.4	7.1%	3.2%
anti-c	4	27	16	1.7	6.1%	5.3%
anti-C	-	21	9	2.3	4.3%	6.2%
anti-Fya	5	17	10	1.7	3.8%	4.9%
anti-Lua	1	11	13	0.8	3.4%	-
anti-Cw	-	11	8	1.6	2.7%	3.1%
anti-Kpa	3	13	3	4.3	2.3%	-
anti-D	-	11	4	2.8	2.1%	11.4%
anti-Jkb	-	10	5	2.0	2.1%	0.8%
anti-Wra	3	8	5	1.4	1.8%	6.0%
anti-M	0	6	5	1.2	1.6%	9.6%
anti-S	3	5	5	1.0	1.4%	2.0%
anti-Fyb	3	7	2	3.5	1.3%	0.5%
anti-e	-	4	2	2.0	0.8%	0.9%

** Total 33; three other antibody reports in this group: 1x anti-P1, 1x anti-Kna & HTLA antibodies and 1x anti-s*
 # From: van Gammeren et al. A national Transfusion Register of Irregular Antibodies and Cross (X)-match Problems: TRIX, a 10-year analysis. TRANSFUSION 2019;59;2559-2566.

Table 22 Reports of formation of anti-D, anti-c, anti-E and anti-K in women <45 years old in 2020

Antibody	2020		2019
Anti-D	none		none
Anti-c	4	3× transfusion ≤ 2011 1× emergency situation	none
Anti-E	5	1× calculated risk with stem cell transplantation 4× transfusion ≤ 2011	7
Anti-K	2	1× IBCT (2020, see Table 10) 1× transfusion ≤ 2004	2

Other reaction

Transfusion reaction which does not fit into the categories above.

- After new allo-antibody formation, other reaction was the reporting category with the highest number of reports in 2020: 317 including three other reactions registered with incidents (2x other incident, 1x incorrect blood component transfused).
- Since 2010, one of the three largest categories of reports of transfusion reactions with severity grade 2 or higher and definite, probable or possible imputability, 30 in 2020 (18 in 2019). The largest increase in severe reactions (from 1 to 9) concerned reactions with hypotension as most prominent symptom.
- Increase in other reaction with dyspnoea or decrease in oxygen saturation (Table 23). Some of these were non-hemolytic reactions accompanied by respiratory deterioration that required clinical intervention. Other reports in this group include reactions with dyspnoea/decrease in oxygen saturation as the most prominent feature, but which did not meet the criteria for TRALI, TACO or anaphylactic reaction and which could not be diagnosed as TAD because there were other possible explanations for respiratory deterioration.

- The breakdown into subtypes in 2020 also shows an larger number of reactions where a finding other than dyspnoea or increase in blood pressure prevented the reaction from being classified in a standard reporting category (e.g. a positive blood culture that had been present previously and was detected again at the time of the reaction or an increase in temperature that lasted longer than 24 hours).
- For 16 reactions, for which it was judged that the symptoms still fitted into the relevant category, an additional category of other reaction was registered to signal findings such as increase in blood pressure with febrile reactions, insufficient yield of a platelet transfusion, an increase in temperature lasting longer than 24 hours or a repeat positive blood culture result in a patient with TACO.

Table 23 Types of reactions that are registered as other reaction
(broken down as in previous TRIP reports)

Type of reaction	2019	2020	2020 Def., Prob.	2020 Possible	2020 ≥grade 2*
Reactions with hypotension	58	57	10	38	10
Subgroup hypotensive reaction (ISBT)#	8	14	2	11	7
Reactions with dyspnoea	23	67	9	43	6
Increase in blood pressure	30	31	8	22	1
(possibly) cardiac	21	19	2	14	3
Did not fully comply with TRIP definitions standard category	46	90	17	53	5
Other symptoms	79	53	8	35	5
Total	**257**	**317**	**54**	**205**	**30**

Abbreviations: Def., Prob. = Imputability definite or probable
** Imputability definite, probable or possible*
 # For this, systolic blood pressure must be ≤80 mm Hg

Other reaction case descriptions of 2020 reports can be found in the Report of the Month (Melding van de maand) series on www.tripnet.nl:
Report of the month April 2020: Were preventive measures successful in preventing TACO?

Conclusion Other reaction
The increased number of other reactions is mainly found in the subgroups with dyspnoea and 'did not fully comply with TRIP definitions'. It is possible that this is related to the population of hospital patients in 2020 due to the COVID-19 pandemic. Serious other reactions include, in particular, reactions with hypotension.

3.3 Infectious transfusion

Bacterial problems associated with blood transfusion

Post-transfusion bacteremia/sepsis
Clinical symptoms of bacteremia/sepsis arising during, directly after or some time subsequent to a blood transfusion, for which there is a relevant positive patient blood culture result and a causal link to a transfused component may or may not be confirmed.

Bacterial contamination of blood component

Relevant numbers of bacteria in a (remnant of) blood component or in the bacterial screen bottle of a platelet component, or in material from the same donation, demonstrated by approved laboratory techniques, preferably including typing of the bacterial strain or strains.

- A total of 73 reports of Post-transfusion bacteremia/sepsis, compared to 84 in 2019, including late reports (Tables 24 and 25)
- Number of reporting hospitals: 37 (46%), 1-12 reports per hospital
- The number of serious reports of Post-transfusion bacteremia/sepsis (grade 2 and higher) with definite, probable or possible imputability is 10, compared to 8 in 2019.
- None of the reports of Post-transfusion bacteremia/sepsis met the criteria for TTBI in 2020, see Figure 14.
- Post-transfusion bacteremia/sepsis was reported four times as an additional category associated with TACO
- Bacterial contamination of blood product was reported nine times: 2x in cases of Post-transfusion bacteremia/sepsis (Table 26), 1x with Mild non-haemolytic fever reaction, 6x with Other reaction.

Table 24 Overview of reports from hospitals relating to bacterial problems 2016-2020

	2016	2017	2018	2019	2020
Post-transfusion bacteremia/sepsis (cases of TTBI, as assessed by experts)	64	72	72	84	73
	(3)	(2)	(1)	(1)	(0)
Post-transfusion bacteremia/sepsis as additional category (not TTBI)	2	5	1	0	5
Bacterial contamination of blood component* (including reports of positive bacterial screening)	10	4	0	1	0
Bacterial contamination of blood component (including reports of positive bacterial screening) as an additional category	16	19	11	12	9

** The cases in which bacterial screening by the blood establishment results in a positive culture are supplied to TRIP in the form of a single total figure by Sanquin, and since 2017 have only been registered for TRIP reporting as a separate report by a hospital if a patient showed symptoms or experienced negative consequences, such as postponement of surgery or the administration of prophylactic medication.*

Table 25 Overview of reports of Post-transfusion bacteremia/sepsis

Number of reports	73	
Age average, median (IQR)	57 years, median 67 (IQR 47.5-76.5)	
Sex	32 Female (44%)	
Serious	14 serious, including 10 with definite, probable or possible Imputability	
Product	**Number (% of total)**	**Reports per 1000 units**
Red blood cell concentrate	63 (86%)	0.16
Platelet concentrate	7 (10%)	0.13
FFP	0	
SD-plasma	0	
Convalescent anti-COVID-19 plasma	0	
Multiple types (labile and possibly SD-plasma)	3 (4%)	
Symptoms (number of reports):		
Increase in temperature: 1-2 ˚C	32	
≥2 ˚C	35	
Chills	39	
Dyspnoea/decrease in oxygen saturation/tachypnoea	18	
Decrease in blood pressure	8 (5x ≥20 mm Hg syst and/or diast)	
Increase in blood pressure	9 (7x ≥20 mm Hg syst and/or diast)	
Tachycardia	18	

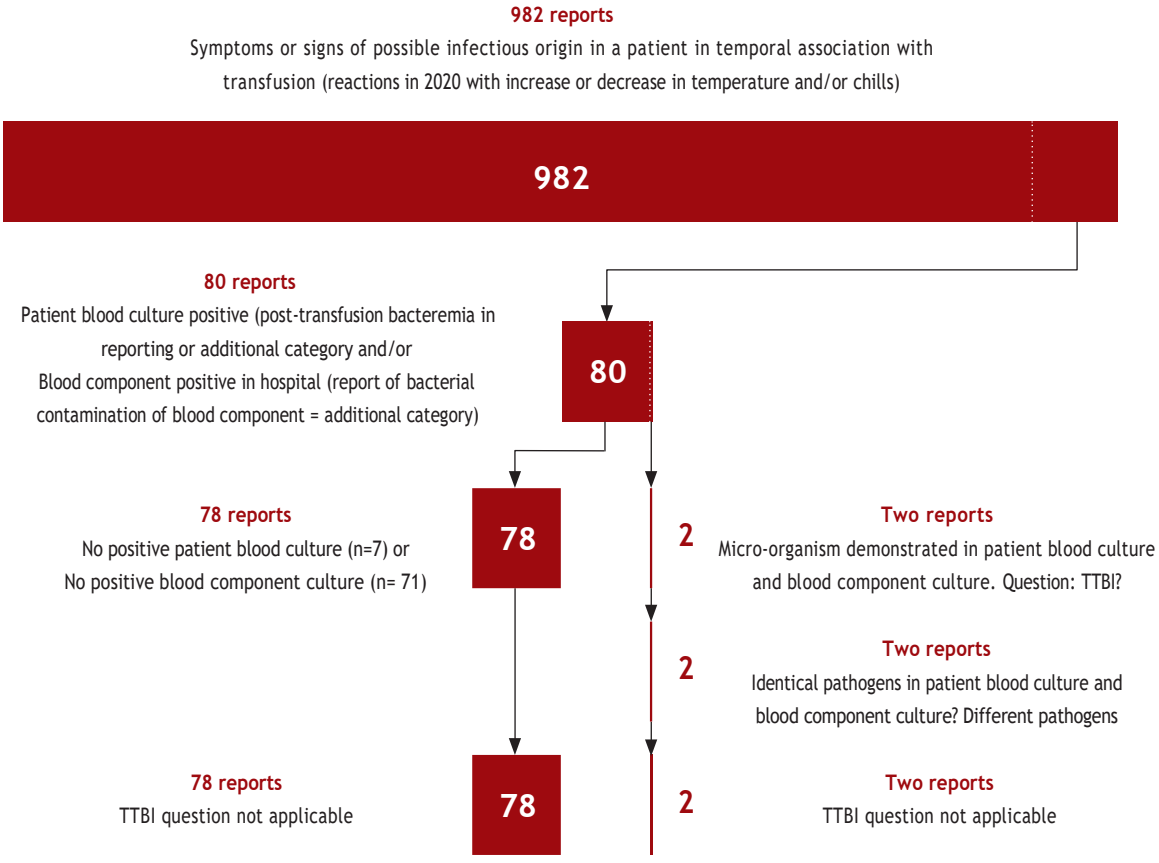

Figure 14 Is it a case of transfusion-transmitted bacterial infection (TTBI)?

Table 26 Overview of bacteriological screening of platetet concentrates by Sanquin

Number of units (Sanquin)	2016	2017	2018	2019	2020
PLTs with initial positive result	218	188	185	185	183
Number already transfused (PLTs and associated RBCs)	79	96	100	81	84*

** In three cases Sanquin was informed that a mild reaction had been observed in the patient, but the reaction was not linked to the positive result of the bacteriological screening; in five cases Sanquin did not receive a response from the hospital.*
Abbreviations: PLTs=platelets; RBCs=red blood cells

Post-transfusion viral infection (n=0 in 2020; 2021 definition)
Demonstration of a viral infection in a transfused patient within a period corresponding to the incubation period of that infection, leading to investigation of a possible a causal link to a transfused unit

Information from hospitals
TRIP did not receive any reports of post-transfusion viral infection in 2020.

Look-back by the supplier/recall* (2020 definition)
Retrospective notification of a non-compliant or possibly infectious donation (other than bacterial contamination of a blood component), leading to investigation of the recipient for that infection or possible consequences.
*Note: If there was a notification from Sanquin but the patient had no reaction or other (medical) consequences (such as prophylactic medication), hospitals should not report these cases to TRIP.

Information from hospitals
As of 2020, hospitals are requested to only report look-backs and recalls to TRIP if there are consequences for the patient, such as a reaction, prolongation of hospitalization, additional treatment, et cetera). One report concerning a look-back was registered: blood tests were performed in 2020 on a patient with a low follow-up frequency, ruling out hepatitis B transmission after transfusion in 2017.

Information from Sanquin
In 2020, look-back investigations were performed according to protocol after 7 seroconversions (1x HBV; 6x Syphilis). Hospitals were requested to trace the recipients in order to inform them (look-back); no transmissions were found. The investigation following one seroconversion report in 2019 that had not yet been completed at the time of drafting the report also showed no transmission.

Conclusion Infectious transfusion complications
TRIP received no report of a transmitted viral infection in 2020. In 2020 there were also no reports of post-transfusion bacteremia/sepsis in which transfer of a bacterial infection through a blood component was confirmed by the detection of the same bacterial species in the patient's blood culture as in the culture of the blood component. Alertness and timely investigations remain necessary in order to provide appropriate treat ment to patients with symptoms that could indicate sepsis.

3.4 Blood management techniques

In 2020, TRIP received no reports from hospitals concerning transfusion reactions or incidents related to the use of blood management techniques, such as reinfusion drains or cell savers.

3.5 Reports associated with SD-plasma

Use of SD-plasma in the Netherlands
SD stands for solvent-detergent, a pharmaceutical virus reduction method which is applied to pools of donor plasma units. In 2014-2016, Omniplasma®, which is an SD-plasma produced from Dutch plasma donations collected by Sanquin, was progressively rolled out as the standard plasma product for transfusion. Sanquin continues to supply FFP for pediatric use and other special indications.

Because SD-plasma has the legal status of a pharmaceutical product, hospitals draw up contracts between the hospital pharmacy and the blood transfusion laboratory. In accordance with arrangements made between TRIP and Lareb, the Dutch pharmacovigilance agency, reports of transfusion reactions and/ or transfusion incidents may be submitted using the TRIP system. As of 2018, TRIP forwards such reports of reactions to Lareb, with the exception of new allo-antibody formation in patients who were also administered cellular components and incidents not related to component quality. (The reporting to Lareb includes cases in which labile blood components were also administered). After the reports have been coded according to pharmacovigilance practices, the reports are transferred to the European database Eudravigilance. At the same time, the TRIP annual hemovigilance reports continue to provide a complete picture of the transfusion chain.

Figure 1 on page 8 shows the course of the use of SD-plasma. The 27 reports with SD-plasma from 2020 are summarized in Table 26 (2019: 31 reports). The categories which represent the largest numbers of reactions are the allergic reactions (anaphylactic and other allergic reactions), as was previously the case for FFP. The general picture is comparable to when FFP was the standard plasma product.

Table 27 Reports associated with SD-plasma in 2020

	Non-serious reactions		Serious reactions	
Type of reaction	SD only	SD and other bc	SD only	SD and other bc
Anaphylactic reaction	1		2	1
Other allergic reaction	3	1		
Mild non-hemolytic TR	2	1		
Non-hemolytic TR		1		
New allo-antibody formation		3		
Other reaction	2	1		
Post-transfusion bacteremia/sepsis		1		
Transfusion-associated circulatory overload	1	2		
TRALI				1
Incidents				
Other incident*		1		
Incorrect blood component transfused#	1	2		

** Three units were wasted: because of massive blood loss, eight units were ordered, but only five were administered.*
 # 1x blood group A instead of AB selected for AB patient, 1x administration based on laboratory results on the correct sample but under the identity of another patient, 1x unit administered that was intended for another patient.

Conclusion
The side effects of the use of SD-plasma (Omniplasma®) are similar to the reactions previously reported to TRIP with the use of quarantine fresh frozen plasma.

4 GENERAL

4.1 TRIP working methods and participation in TRIP reporting

A central registration system for blood transfusion reactions and incidents makes it possible to monitor the transfusion chain, detect weak links and make recommendations for improving transfusion safety. The incidence of known side effects of blood transfusions is tracked and previously unknown reactions to transfusion of current or new blood products can be detected in timely fashion.

The TRIP foundation (Transfusion (and Transplantation) Reactions In Patients) was created in 2001 by representatives of the various professional societies involved in blood transfusion. The national TRIP Hemovigilance and Biovigilance Office has operated a registry for transfusion reactions and incidents since 2003 in collaboration with the contact persons in the hospitals and the national blood service, Sanquin. . Since August 2006 TRIP has also run a national reporting system for serious adverse reactions and events in the chain of clinical application of human tissues and cells (biovigilance). The biovigilance findings are reported in a separate annual biovigilance report which is also available on www.tripnet.nl under publications/reports. TRIP is advised by the Hemovigilance and Biovigilance Advisory Boards, which consist of representatives of the professional societies.

Reporting to TRIP is anonymous. Though voluntary in principle, it is regarded as the professional standard by the Healthcare Inspectorate (Inspectie Gezondheidszorg en Jeugd, IGJ) and the national Blood Transfusion Policy Guideline 2020. Reporting to TRIP is separate from the hospitals' responsibility to

Reporters of transfusion reactions and incidents are asked to provide results of relevant investigations and grade the clinical severity of the reaction. The imputability, i.e. the likelihood that the reaction can be ascribed to the administered transfusion, is also assessed. If necessary, TRIP requests further explanation or details from the reporter. This enables the TRIP physicians to assess their coherence and verify the reporting category of potentially serious reports. An Expert Committee (EC), consisting of experts from the Hemovigilance Advisory Board, advises on the classification of serious and complex reports.

Under the requirements of European Directive 2002/98/EC it is mandatory to report serious adverse reactions and incidents which could have a relation to quality and/or safety of blood components. In the Netherlands, these requirements have been implemented in the Quality, Complaints and Disputes in Healthcare Act (Wet kwaliteit, klachten en geschillen zorg, Wkkgz), under the heading of "hospital blood banks" (Ziekenhuisbloedbanken), section 5.1, paragraph 3. The hospitals can send serious reports to the Healthcare Inspectorate and Sanquin using the TRIP online reporting system. TRIP performs the analysis of these reports for the competent authority, the Ministry of Health, Welfare and Sports (MoH), and the healthcare inspectorate. TRIP compiles the annual mandatory overview of serious adverse events and reactions to be forwarded to the European Commission, via the Ministry of Health, Welfare and Sport.

At the end of each reporting year TRIP receives a copy of Sanquin's annual overview of serious adverse reactions and serious adverse events as reported to the healthcare inspectorate, as well as numbers of distributed blood components. Each year TRIP and Sanquin match up relevant serious reports which have been reported through different routes using anonymous details (date of transfusion, age, sex, type of blood component and general type of reaction), the intention being to ensure that the information in the TRIP database is as complete as possible. With regard to reactions in 2020, two reports of serious transfusion reactions (TRALI), which had been reported to Sanquin, could not be found in the TRIP database in March 2020. TRIP urgently requests hospitals to always report a reaction to TRIP as soon as possible after reporting it to Sanquin. If all reports to Sanquin are sent through the TRIP reporting system this will ensure

that they can be matched and that Sanquin always has access to the final classification (diagnosis) of each reaction in the TRIP system.

The value of reporting and collecting transfusion reactions and incidents at the national level depends on the participation of all the reporting establishments. In 2020, TRIP received reports from 72 hospitals. Four hospitals indicated that there had been no reports of incidents or reactions in the TRIP reporting categories in 2020. Five hospitals had not provided any information about reports or numbers of transfusions to TRIP at the time of compiling this report. The level of participation among hospitals is 76/81=94% for submitting reports and 79/81=98% for submitting data on the number of blood components transfused. Two of the hospitals submitted their reports after the closing date and are therefore not included in the participation figure for reports.

Besides the hospitals, TRIP is in contact with eight private clinics which have been licensed by the Ministry of Health, Welfare and Sport (VWS) to receive and transfuse blood components to their patients. Five of the licensed institutions submitted data in 2020, of which four reported that they had not administered any blood products in 2020 and one institution had administered two units to one patient in 2020. The institutions informed TRIP that the figures on blood components and reports of any reactions would be made by the transfusion labs with which they have contracts

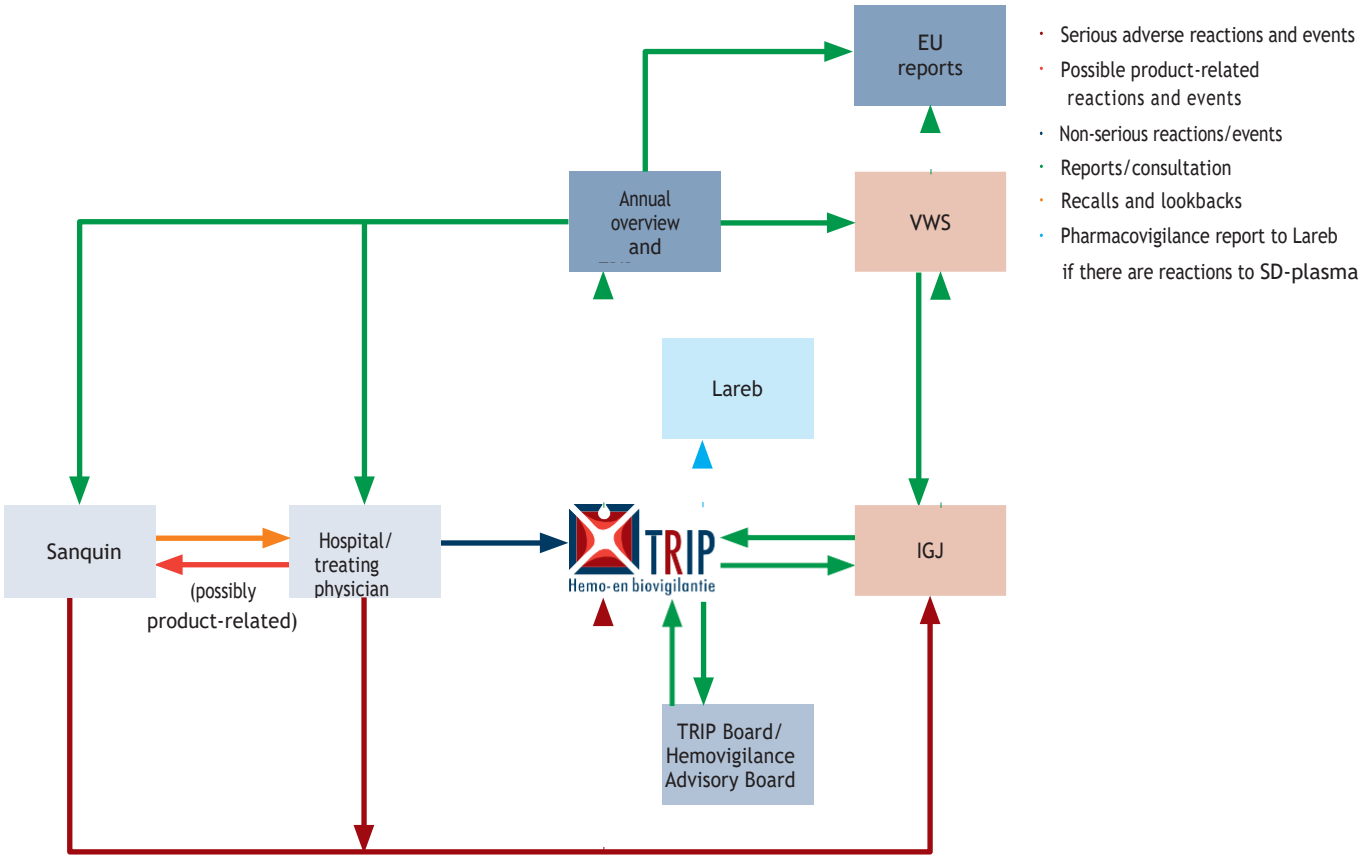

Figure 15 Flow of hemovigilance information and outputs

APPENDIX

LIST OF TERMS AND ABBREVIATIONS

AHTR	Acute hemolytic transfusion reaction
AIHA	Autoimmune hemolytic anaemia
Bc	Blood component
BG	Blood group
BMT	Blood management techniques
BNP	Brain-type natriuretic peptide
CCP	COVID-19 convalescent plasma
COVID-19	Coronavirus disease 2019
CT	Computed tomography (imaging)
DHT	Delayed hemolytic transfusion reaction
EU	European Union
FFP	Fresh frozen plasma
Hb	Hemoglobin
IBCT	Incorrect blood component transfused
ICU	Intensive care unit
IGJ	Healthcare Inspectorate
IQR	Interquartile range
Irrab	Irregular antibodies
Mild NHFR	Mild non-hemolytic febrile reaction
NHFR	Non-hemolytic transfusion reaction
NM	Near miss
OI	Other incident
PLT	Platelet concentrate
Post-Tf bact/sepsis	Post-transfusion bacteremia/sepsis
Pt	Patient(s)
RBC	Red blood cell concentrate
Rh	Rhesus (blood group)
Sanquin	Sanquin (Dutch national blood establishment)
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SCT	(hematopoietic) stem cell transplantation
SD	solvent-detergent (a pathogen reduction method)
TA-GVHD	Transfusion-associated graft versus host disease
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea (TAD)
Tf	Transfusion
TR	Transfusion reaction
TRALI	Transfusion-related acute lung injury
TRIP	TRIP Foundation (Transfusion and Transplantation Reactions In Patients)
TRIX	Transfusion Register of Irregular antibodies and X(cross-match) problems
TTBI	Transfusion-transmitted bacterial infection
VWS	Dutch Ministry of Health, Welfare and Sport

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